



ESCOLA UNIVERSITÁRIA VASCO DA GAMA

MESTRADO INTEGRADO EM MEDICINA VETERINÁRIA

**PERCEPTION OF PORTUGUESE VETERINARIANS ON THE CLINICAL APPLICATION OF
PSYCHOACTIVE DRUGS AND ITS PSYCHOPHARMACOLOGICAL ACTIVITY IN DOGS AND CATS**

Pedro Miguel Figueiredo de Almeida
Coimbra, setembro de 2020



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Pedro Miguel Figueiredo de Almeida

Aluno do Mestrado Integrado em Medicina Veterinária

Constituição do Júri

Presidente do Júri: Prof. Doutora Sofia Duarte

Arguente: Prof. Doutor Gonçalo da Graça Pereira

Orientador: Prof. Doutora Ana Catarina Figueira

Orientador Interno

Prof. Doutora Ana Catarina Figueira

Coorientadores Internos

Mestre Maria Isabel Santos

Prof. Doutor Hugo Vilhena

Orientadores Externos

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Table of Contents

Acknowledgements	iv
List of Figures	vi
List of Tables	vii
List of Acronyms and Abbreviations	viii
Resumo	2
Abstract.....	3
1. Introduction	4
2. Materials and methods	6
2.1. Questionnaire	6
2.2. Online platform	6
2.3. Participants	6
2.4. Statistical analysis	7
3. Results.....	8
3.1. Portuguese veterinarians' characterization	8
3.2. Animal behaviour implementation aspects of veterinary medical centres	9
3.3. Familiarity with animal behaviour concepts and psychopharmacology	9
3.4. Frequency of animal behavioural problems presentation	10
3.5. General acquaintance with psychoactive medication	10
3.5.1. Frequency of psychoactive drug prescriptions	10
3.5.2. General use of psychoactive drugs	11
3.6. Specific choices of psychoactive drugs	13
3.6.1. Acute stress situations.....	13
3.6.2. Fractionous behaviours	14
4. Discussion	16
5. Conclusions	19
6. References	20
Appendix.....	23
Appendix I – List of psychoactive drugs used in dogs for behavioural veterinary medicine.	24
Appendix II – List of psychoactive drugs used in cats for behavioural veterinary medicine.	25
Appendix III – Questionnaire: Portuguese veterinary class perception about psychoactive drugs and its use and its pharmacological activity in dogs and cats.....	26
Appendix IV – List of currently approved psychoactive drugs for behavioural veterinary medicine in Portugal and their summary of product characteristics.	36

List of Figures

Figure 1 - Frequency of psychoactive drug use for behavioural problems in dogs and cats.

Figure 2 - Oral psychoactive medication choices for acute stress situations in dogs.

Figure 3 - Oral psychoactive medication choices for acute stress situations in cats.

Figure 4 - Psychoactive medication choices in dogs presenting fractious behaviours.

Figure 5 - Psychoactive medication choices in cats presenting fractious behaviours.

List of Tables

Table 1 - Portuguese veterinarians' characterization.

Table 2 - Animal behaviour implementation aspects of veterinary medical centres.

Table 3 - Familiarity with the animal behaviour concepts and psychopharmacology.

Table 4 - Frequency of animal behavioural problems presentation.

Table 5 – Frequency of psychoactive drug prescriptions.

Table 6 – Use of phenothiazines in managing stress and anxiety in veterinary medical centres.

List of Acronyms and Abbreviations

BZD – Benzodiazepine

DGAV – Direção Geral de Alimentação e Veterinária

EUVG – Escola Universitária Vasco da Gama

FMV-UL – Faculdade de Medicina Veterinária – Universidade de Lisboa

ICBAS-UP - Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

MAOI – Monoamine oxidase inhibitor

OMV – Ordem dos Médicos Veterinários

OTM – Orotransmucosal

PsiAnimal - Associação Portuguesa de Terapia do Comportamento e Bem-Estar Animal

SARI - Serotonin antagonist and reuptake inhibitor

SSRI – Selective serotonin reuptake inhibitor

TCA - Tricyclic antidepressant

UTAD - Universidade de Trás-os-Montes-e-Alto-Douro

PERCEPTION OF PORTUGUESE VETERINARIANS ON THE CLINICAL APPLICATION OF PSYCHOACTIVE DRUGS AND ITS PSYCHOPHARMACOLOGICAL ACTIVITY IN DOGS AND CATS

Pedro Almeida^a, Maria Isabel Santos^{a,b}, Hugo Vilhena^{a,c,d}, Nuno Carolino^{a,e}, João Araújo^f, João Pedro Monteiro^{b,f,g}, Ana Catarina Figueira^{a,h}

^aCentro de Investigação Vasco da Gama (CIVG), Departamento de Ciências Veterinárias (DCV) / Escola Universitária Vasco da Gama (EUVG), Avenida José R. Sousa Fernandes 197, Campus Universitário- Bloco B, Lordemão, 3020-210 Coimbra, Portugal (pedrofig.almeida@gmail.com; misantos_be@sapo.pt; hcrvilhena@hotmail.com; carolinonuno@hotmail.com; acfigueira@gmail.com)

^bAssociação Portuguesa de Terapia do Comportamento e Bem-Estar Animal (PsiAnimal), Rua Veloso Salgado, nº 23 R/C Esquerdo, 1600-216 Lisboa, Portugal

^cHospital Veterinário Baixo Vouga (HVBV), Estrada Nacional 1, 355, 3750-742 Segadães-Águeda, Portugal

^dCentro de Ciência Animal e Veterinária (CECAV), Universidade de Trás-os-Montes e Alto Douro (UTAD), Quinta de Prados, 5001-801 Vila Real, Portugal

^eInstituto Nacional de Investigação e Veterinária (INIAV), Avenida da República, Quinta do Marquês, 2780-157 Oeiras, Lisboa, Portugal

^fHospital Veterinário do Bom Jesus (HVBj), Avenida General Carrilho da Silva Pinto, 52, 4715-380 Braga, Portugal (joaoaraujo.hvbj@gmail.com; joapedromonteiro@outlook.com)

^gInstituto de Ciências Biomédicas Abel Salazar - Universidade do Porto (ICBAS-UP), R. Jorge de Viterbo Ferreira 228, 4050-313 Porto, Portugal

^hHospital Veterinário Universitário de Coimbra (HVUC), Avenida José R. Sousa Fernandes 197, Campus Universitário- Bloco B, Lordemão, 3020-210 Coimbra, Portugal

Resumo

Ansiedade, medo, stresse agudo e comportamentos de reatividade são estados emocionais que os médicos veterinários precisam de saber reconhecer e minimizar em ambiente clínico. Quando o bem-estar de um cão ou de um gato está comprometido, existem fármacos psicofarmacológicos que podem ser utilizados. Os objetivos principais deste estudo foram avaliar o conhecimento de psicofarmacologia, as medicações psicotrópicas com as quais estão familiarizados e as classes de medicação psicotrópica oral usadas para reduzir níveis de ansiedade e agressividade na prática clínica em cães e gatos, por veterinários Portugueses que se encontram atualmente a trabalhar na área de animais de companhia. Para tal, foi distribuído um questionário à classe médico veterinária Portuguesa. Foram obtidos duzentos e quarenta e um questionários válidos. Os resultados indicam que embora os médicos veterinários Portugueses afirmem ter conhecimento em comportamento animal (92,5%) e atendam cães e gatos com problemas comportamentais (94,7% e 95,5%, respetivamente), ainda desconhecem conceitos psicofarmacológicos básicos. A acepromazina é indevidamente utilizada em cães e gatos para controlo de stresse agudo (18,5% e 15,5%, respetivamente). Na presença de comportamentos agressivos, a escolha principal é a de protocolos anestésicos injetáveis em ambas espécies. A dexmedetomidina por via orotransmucosal e benzodiazepinas por via oral (em cães) e de gabapentina e benzodiazepinas por via oral (em gatos) foram prevalentemente prescritas para reduzir níveis de stresse agudo na clínica. Conclui-se que a psicofarmacologia aplicada a comportamento animal ainda não é muito utilizada em Portugal, recorrendo-se muito ao uso de acepromazina e de protocolos anestésicos injetáveis. Existe ainda uma necessidade de prosseguir investigação no sentido de proporcionar aos médicos veterinários mais ferramentas para uma redução efetiva de stresse e ansiedade no cão e no gato em ambiente clínico.

Palavras-chave: acepromazina, ansiedade, benzodiazepinas, cão, gato, médico veterinário, psicofármacos, stresse agudo

Abstract

Anxiety, fear, acute stress and reactive behaviours are emotional states that veterinarians must be able to recognize and reduce in clinical environment. When the welfare of a dog or cat is compromised, there are useful psychopharmacological drugs that can be used. The main objectives of this study were to evaluate the knowledge on psychopharmacology, the psychoactive medications they are familiarized with and which classes of oral psychoactive drugs are used to reduce anxiety and fractious behaviours in dogs and cats by Portuguese veterinarians, currently working in small animal practice. For that purpose, a questionnaire was distributed among the Portuguese veterinary class. Two hundred and forty-one valid answers were obtained. The results show that even though most Portuguese practitioners (92,5%) stated to have knowledge in animal behaviour field and to receive dogs and cats with behaviour problems (94,7% and 95,5%, respectively), basic psychopharmacologic concepts are still unknown. Acepromazine is highly misused in dogs and cats in acute distress situations (18,5% and 15,5%, respectively). In the presence of fractious behaviours, injectable anaesthetic protocols are the main choice in both species. Orotransmucosal dexmedetomidine and oral benzodiazepines (in dogs) and oral gabapentin and benzodiazepines (in cats) were prevalingly prescribed to reduce acute stress levels in clinical environment. It was concluded that psychopharmacology applied to animal behaviour is still underused in Portugal, with a high resort to acepromazine and injectable anaesthetic protocols. There is a need to further investigate, in order to give veterinarians more tools in effectively reducing anxiety and stress levels in dogs and cats in a clinical environment.

Keywords: acepromazine, acute stress, anxiety, benzodiazepines, cat, dog, psychoactive drugs, veterinarian

1. Introduction

Visits to veterinary clinics are essential to our domestic dogs' and cats' health and welfare, however, it can also stand as a very stressful experience for our companion animals. It is frequent that the conjugation of an unfamiliar environment, noises and smells (to which they might have already created negative associations) and the confrontation with unknown humans and other animals trigger emotions like fear and anxiety (Döring et al., 2009; Mariti et al., 2015). A study by Stanford (1981), that intended to study the behaviour of 462 dogs entering a veterinary clinic, stated that 70% were unwilling to enter and the majority showed submissive or fearful behaviours. Also, around 60% showed signs of anxiety and 18% fear-induced aggression. In a similar, and more recent study done by Bamberger & Houpt (2006) in 1,644 dogs, the main reported problems were still several types of aggression (72,4%) and signs of generalized and separation anxiety (19,7%).

A negative veterinary experience can have long-term impacts not only for companion animals, but also to the owners. Many pet owners find taking their animal to the veterinarian as a highly stressful experience, especially in cats. The attitudes taken inside the veterinary clinic will directly affect the owner's decisions and how often they'll visit (Volk et al., 2011). Additionally, if not properly attended, anxious/fearful animals can injure themselves or others at the veterinary clinic. Addressing fear, anxiety and promoting animal friendly practice is crucial to improve the welfare of companion animals within a veterinary clinical environment (Edwards et al., 2019).

Although fear and anxiety have physiologic responses that overlap, it is important for veterinarians to understand and distinct one from another. Fear is, by definition, an emotion that induces an animal to avoid certain situations or activities that it perceives as dangerous. It is considered a normal behaviour and an adaptive response that helps the animal escape undesired outcomes (Lloyd, 2017). Most people recognize overtly fearful behavioural responses. In dogs, tucking the body and limbs, trembling, hiding and averting eyes are the most common. Fearful cats might tend to lower their heads, lean back and move their ears down/back in an attempt to make themselves smaller, but when in a high fearful state or unable to run away, cats are more likely to hiss and react aggressively (Yin, 2009a). In extreme cases on both species, urination, defecation, release of anal sacs and fear induced aggression are described. The determination of whether the fearful response is abnormal or inappropriate must always be determined by its context (Overall, 2013a). Anxiety is an unspecific response to a prospective stimulus, like an apprehensive anticipation of future danger, that might be real or imaginary, producing most of the times non-adaptive responses. A chronic and continuous state of anxiety should always be considered an abnormal behaviour and a welfare concern for an animal (Overall, 2013a). To summarize, fear and anxiety can result in similar physiologic responses. In both cases, the activation of the sympathetic autonomic nervous system translates into hypervigilance, increased motor activity, trembling, salivating, hypertension, tachycardia, tachypnoea and/or mydriasis (Yin, 2013).

Psychopharmacology studies how psychoactive medication affects the brain's function, namely its physiology and endocrinology. Psychoactive medication has been used in human psychiatry for several decades and its efficacy has been improving as the interrelationships between brain biochemistry, emotional states and overt behaviour are better understood (Stahl, 2013). Appropriately applied to the field of veterinary medicine, psychoactive drugs can be a useful tool in resolving a pet's behavioural problem or even in decreasing stress levels in an acute distressed state, like at the veterinary clinic. The use of these drugs works as an adjunctive treatment in a behavioural treatment protocol that should always include environmental management and behaviour modification techniques, such as desensitisation and counter-conditioning techniques (Fatjó, 2013; Yin, 2009b). The most commonly used psychoactive drugs nowadays in companion animals are: benzodiazepines (BZDs), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin antagonist and reuptake inhibitors (SARIs) and monoamine oxidase inhibitors (MAOIs) (Crowell-Davis & Dantas, 2019; M. Gruen et al., 2018) (Appendix I and II).

The main goals of this study were to evaluate Portuguese veterinarians' knowledge on psychopharmacology, the psychoactive medication they are familiarized with and which classes of oral psychoactive drugs are used to reduce anxiety and fractious behaviours in dogs and cats. To perform this study, a questionnaire was applied to Portuguese veterinarians currently working in small animal practice.

2. Materials and methods

2.1. Questionnaire

The study's main goals were evaluated through a questionnaire, in a voluntary and anonymous survey, elaborated and distributed on Google Forms® online platform (Appendix III). The survey was available between 1st of March, 2020 and 19th of May, 2020. It consisted of a total of 30 questions, of which 15 were multiple choice, 7 Likert-type scales, 5 check boxes and 3 short answer questions. The survey was trialled by 2 clinical veterinary ethologists that currently work in Animal Behaviour field (namely in referral veterinarian consultations, 1 statistician and 1 general veterinarian practitioner who assessed its feasibility and clarity before distribution to the Portuguese veterinary class.

2.2. Online platform

Google Forms® is an online platform developed by the company Google® (Mountain View, California, USA) which allows the collection of responses from users to a personalized form. All data collected were subsequently stored by this platform and later organized in tables and graphs presented in the results section of this study. Anonymity of responses was guaranteed during the data collection and the processing methods.

2.3. Participants

To be considered eligible for participation in this study, Portuguese veterinarians had to currently be working in small animal practice. Exclusion criteria included veterinarians that were not currently working or were working in other veterinary areas, as well as students or other sort of veterinary staff.

In order to obtain a higher number of answers, the questionnaire was distributed in the following different ways:

- Via e-mail to 641 Portuguese medical centres. The e-mail addresses were consulted in the website of Direção Geral de Alimentação e Veterinária (DGAV), the national authority responsible for animal health in Portugal;
- Via e-mail, followed by a request for distribution, to several higher education institutions of Veterinary Medicine in Portugal, namely Escola Universitária Vasco da Gama (EUVG) in Coimbra, Instituto de Ciências Biomédicas Abel Salazar (ICBAS) - University of Porto in Porto,

Faculdade de Medicina Veterinária (FVM) – University of Lisboa in Lisboa and Faculdade de Medicina Veterinária da Universidade Lusófona de Humanidades e Tecnologias in Lisboa, Universidade de Trás-os-Montes-e-Alto-Douro (UTAD) in Vila Real and Escola de Ciências e Tecnologia in University of Évora in Évora;

- Via e-mail, followed by a request for distribution to their members, to the Associação Portuguesa de Terapia do Comportamento e Bem-Estar Animal (PsiAnimal). PsiAnimal is a non-profit Portuguese association of professionals that work in different areas of animal behavioural therapy and welfare;
- Publication in the veterinary magazine Veterinaria Atual;
- Released in different Portuguese veterinary social media groups.

2.4. Statistical analysis

Data collected from the survey were ordered in Microsoft Excel (Microsoft Corporation®, Washington, USA), before being analysed using Statistical Analysis System® software (SAS Institute Inc.®, North Carolina, USA) through PROC FREQ, to estimate counts and frequencies.

3. Results

Two hundred and forty-one questionnaires were considered valid and analysed in the study. Two hundred and fifty answers were obtained, but 9 were excluded as they were filled by Portuguese veterinarians that weren't currently working in small animal practice. Their answers were subsequently organized in different classes, summarized in Tables 1 to 5, which are detailed below.

3.1. Portuguese veterinarians' characterization

The participants were grouped according to their course's completion year, the demographic region of work and animal species (dog and/or cat) of work (Table 1).

Most veterinarians were graduated in the last ten years and almost all worked with both dogs and cats. Most veterinarians worked in the continental area of Portugal, but there were also responses from veterinarians practising in the country's islands, namely in Madeira (n=1; 0,4%) and in Açores (n=1; 0,4%) (Table 1). Regarding Portuguese veterinarians currently working abroad, eight (3,3%) worked in the United Kingdom and one participant (0,4%) in each of the following countries: Spain, France, Isle of Saint Martin (Netherlands) and the United States of America.

Table 1. Portuguese veterinarians' characterization.

		n	%
Course's completion year	[1979, 2000[	35	14,5
	[2000, 2010[	68	28,2
	[2010, 2020]	138	57,3
Practice's demographic region	North	106	44,0
	Centre	75	31,1
	South	46	19,1
	Islands	2	0,8
	Abroad	12	5,0
Animal species' practice	Dog and cat	239	99,2
	Only dog	0	0
	Only cat	2	0,8

3.2. Animal behaviour implementation aspects of veterinary medical centres

Almost two-thirds (n=158; 65,6%) of the veterinary medical centres in which the participants currently work had no sort of animal friendly concepts in the workplace and nearly the same amount (n=153; 63,5%) had no clinical ethologist responsible for Animal Behaviour consultations and practice (Table 2).

Table 2. Animal behaviour implementation aspects of veterinary medical centres.

		n	%
Animal friendly concepts	Yes	83	34,4
	No	97	40,3
	Not currently, but intends to	61	25,3
Veterinarian Clinical Ethologist	Yes, myself	32	13,3
	Yes, another co-worker	56	23,2
	No	153	63,5

3.3. Familiarity with animal behaviour concepts and psychopharmacology

As demonstrated in Table 3, most participants claimed having fair knowledge in Animal Behaviour field (n=96; 39,8%). Over two-thirds admitted being familiar with psychoactive drugs' effects (n=166; 68,9%).

Table 3. Familiarity with animal behaviour concepts and psychopharmacology.

		n	%
Were you lectured Psychopharmacology during your veterinary education?	Yes	68	28,2
	No	173	71,8
Do you consider having knowledge in the Animal Behaviour field?	Yes	223	92,5
	No	18	7,5
How would you qualify it?	Excellent	11	4,6
	Good	46	19,1
	Fair	96	39,8
	Poor	48	19,9
	Very Poor	22	9,1
Are you familiar with the effect of psychoactive drugs?	Yes	166	68,9
	No	75	31,1

3.4. Frequency of animal behavioural problems presentation

According to the participants, cats are slightly more likely to show behaviour problems than dogs (more than occasionally, 64,4% and 51,5% respectively), as shown in Table 4.

Table 4. Frequency of animal behavioural problems presentation.

		n	%
How often do you receive dogs with behavioural problems?	Almost always	11	4,6
	Frequently	32	13,3
	Occasionally	81	33,6
	Rarely	104	43,2
	Never	13	5,4
How often do you receive cats with behavioural problems?	Almost always	11	4,6
	Frequently	51	21,2
	Occasionally	93	38,6
	Rarely	75	31,1
	Never	11	4,6

3.5. General acquaintance with psychoactive medication

The vast majority of Portuguese veterinarians considered the use of psychoactive medication an asset to improve the welfare status of dogs and cats (n=224; 93%). The participants were asked several questions about their general use of psychoactive medication. Specifically, they were asked about the frequency in which they prescribe it and to indicate the psychoactive drugs they resort to when managing behavioural problems in the dog and cat. On the other hand, a significant number of veterinarians were not familiar with the serotonin syndrome (n=164; 68%) nor with the washout period (n=136; 56,4%).

3.5.1. Frequency of psychoactive drug prescriptions

The frequency of general psychoactive drug prescriptions by Portuguese veterinarians is shown in Table 5. Over two-thirds of veterinarians stated they have never (n=44, 18,3%) or rarely (n=128, 53,1%) prescribed psychoactive medication.

Table 5. Frequency of psychoactive drug prescriptions.

		n	%
How often do you prescribe psychoactive drugs?	Almost always	5	2,1
	Frequently	11	4,6
	Occasionally	53	22,0
	Rarely	128	53,1
	Never	44	18,3

Many veterinarians admitted being familiar with SSRIs and TCAs (n=128, 53,1%; n=165, 68,5% respectively), but regarding the prescription of these specific classes of psychoactive medication most stated they have never (n=143; 59,3%) or rarely (n=64; 26,6%) prescribed SSRIs, with roughly the same number having never (n=104, 43,2%) or rarely (n=92, 38,2%) prescribed TCAs.

3.5.2. General use of psychoactive drugs

The most frequent psychoactive drugs referred by Portuguese veterinarians in dogs and cats with behavioural problems were BZDs (n=224; 93%), phenothiazines (n=222; 92,1%), TCAs (n=195; 80,9%), SSRIs (n=195; 80,9%) and SARIs (n=189; 78,4%). The veterinarians were also asked to indicate the frequency of administration of their drug choices (Figure 1).

Only 18,7% (n=45) of veterinarians referred the use of different psychoactive drugs simultaneously. The most frequent combination was BZDs with SSRIs (n=12; 29,3%), followed by SSRIs with SARIs (n=5; 12,2%).

Over one-third of veterinarians considered that the use of phenothiazines (e.g. acepromazine) has therapeutical effects in the management of behaviour problems in dogs and cats. Their answers are shown in Table 6.

Table 6. Use of phenothiazines in managing stress and anxiety in veterinary medical centres.

		n	%
Do you consider using phenothiazines (e.g. acepromazine) to calm a dog or cat presenting behavioural problems?	Yes	55	22,8
	Yes, but I've never used	30	12,5
	No	111	46,1
	I don't know	45	18,7
Do you consider that phenothiazines have anxiolytic activity in acute stress situations?	Yes	115	47,7
	No	84	34,9
	I don't know	42	17,4

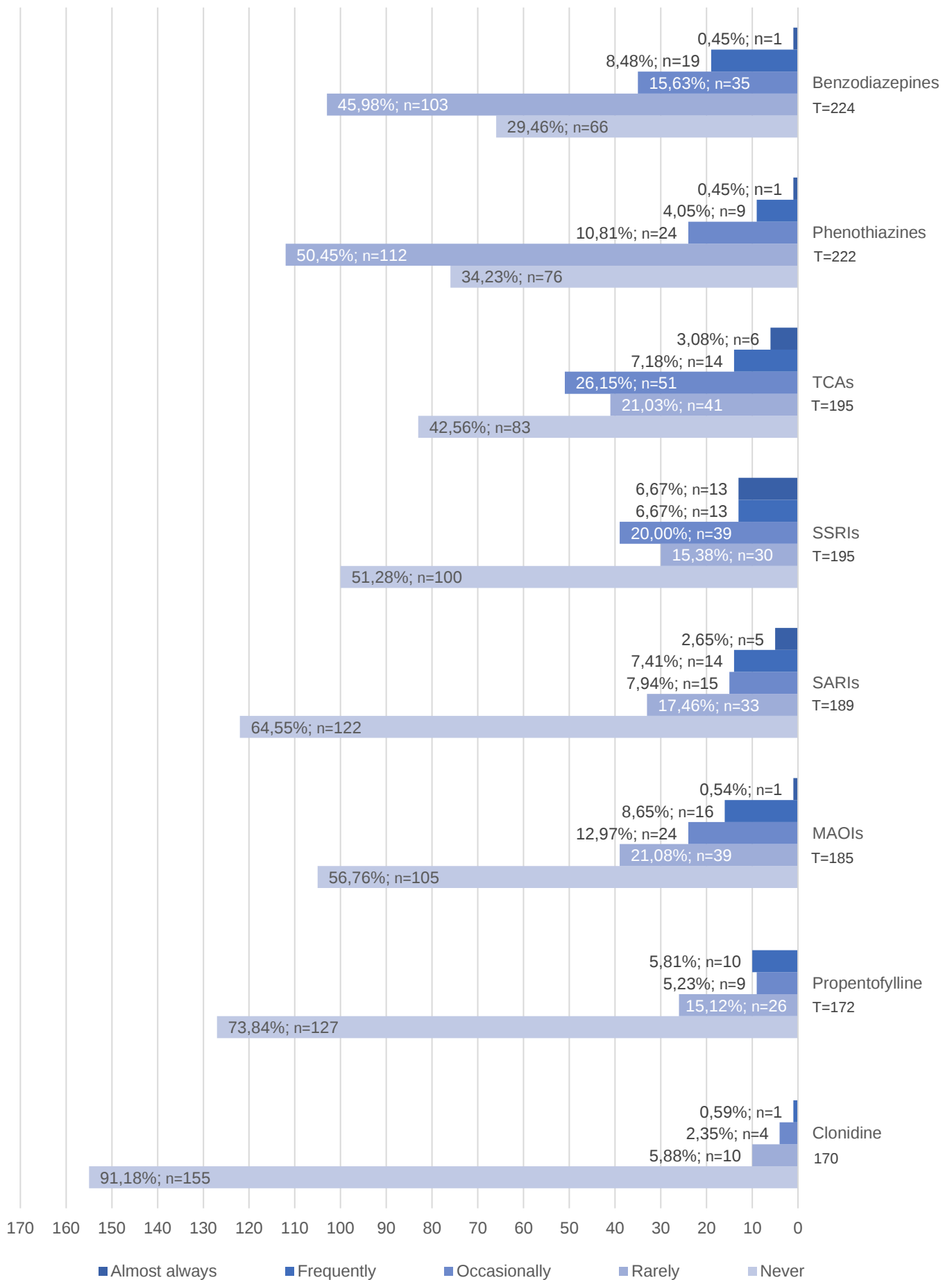


Figure 1. Frequency of psychoactive drug use for behavioural problems in dogs and cats.

3.6. Specific choices of psychoactive drugs

One of the objectives of this study was to determine which classes of oral psychoactive medication Portuguese veterinarians chose to reduce dogs' and cats' levels of stress, fear, anxiety and fractious behaviours in their practice. For that evaluation, they were presented with specific situations which are detailed below.

3.6.1. Acute stress situations

Regarding the psychopharmacological management of acutely distressed dogs in the clinical environment, dexmedetomidine orotransmucosal (OTM) gel, phenothiazines and BZDs were the most frequently chosen. In cats, gabapentin, BZDs and phenothiazines were the top choices. In the category "Others", nutraceuticals and pheromones with calming properties were the most commonly described. Figures 2 and 3 show the preferred oral psychoactive medication in these cases, for each species respectively.

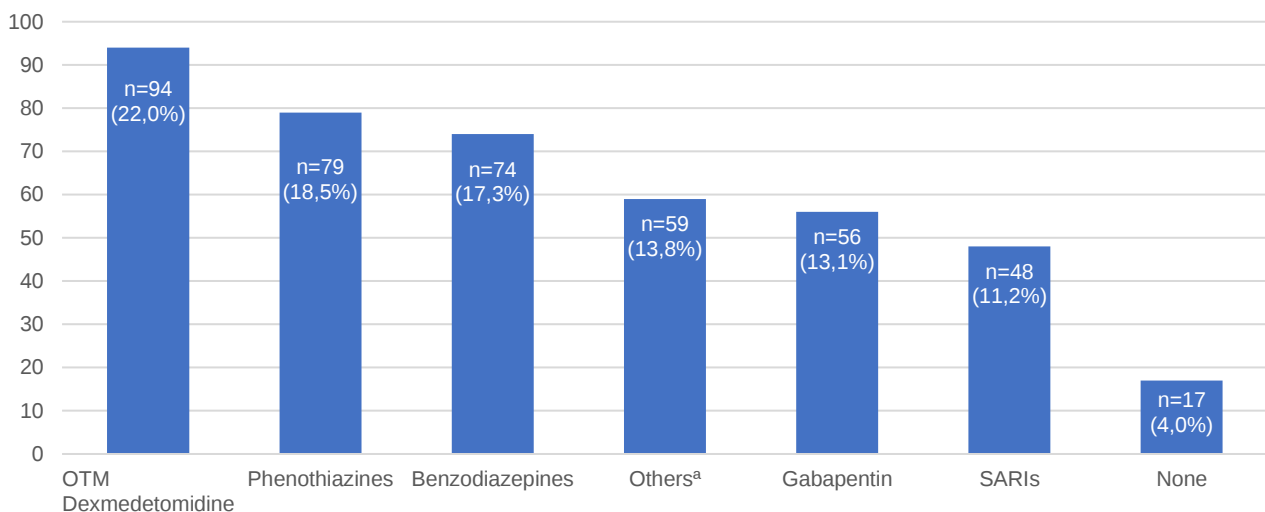


Figure 2. Oral psychoactive medication choices for acute stress situations in dogs.

^a Other substances not classified as psychoactive drugs, such as: nutraceuticals, pheromones and other calming substances were included due to its calming effects. One participant described the use of integrative medicine: homeopathy.

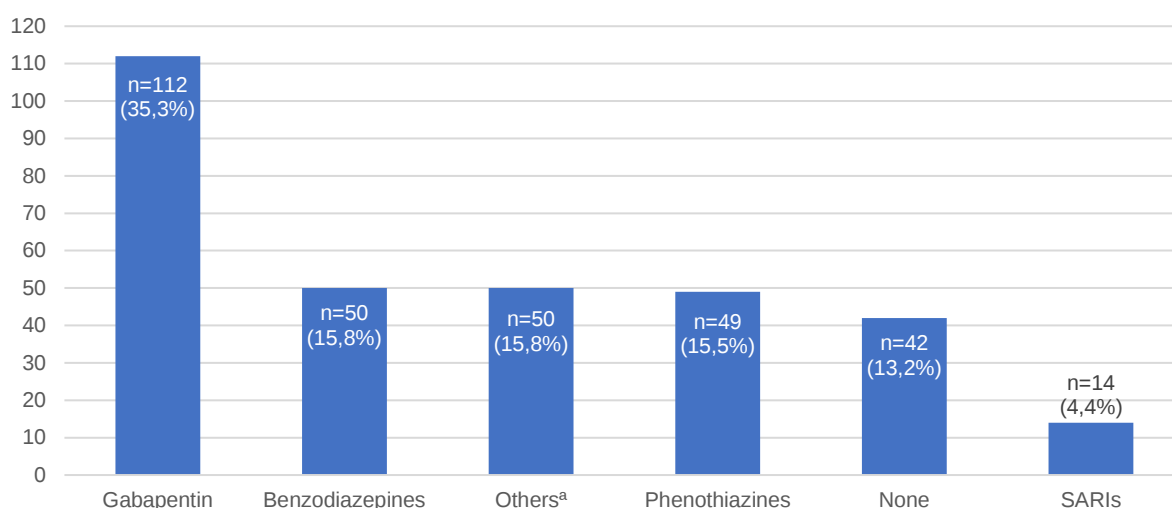


Figure 3. Oral psychoactive medication choices for acute stress situations in cats.

^a Other substances not classified as psychoactive drugs, such as: nutraceuticals, pheromones and other calming substances were included due to its calming effects.

3.6.2. Fractious behaviours

Sometimes dogs and cats, as a response to acute fear or anxiety emotions, may present fractious behaviours towards the veterinary staff, tutors and/or other animals. In the presence of these behaviours most Portuguese veterinarians opt by sedation, using injectable anaesthetic protocols. Figures 4 and 5 show the preferred medications to handle fractious behaviours in clinical environment for each species.

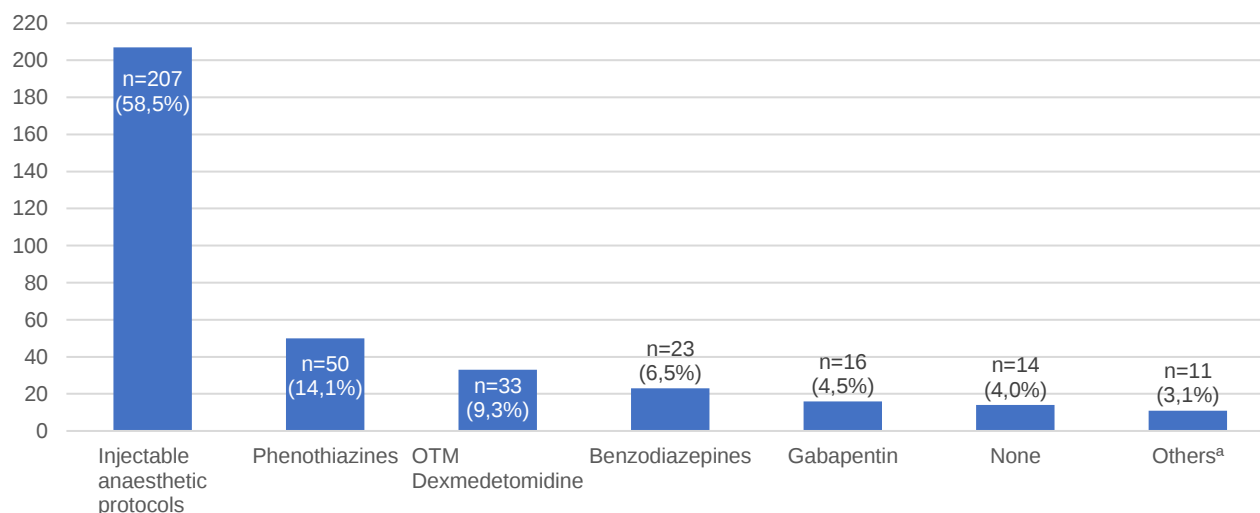


Figure 4. Psychoactive medication choices in dogs presenting fractious behaviours.

^a Trazodone and other substances not classified as psychoactive drugs, such as pheromones, were included due to its calming effects.

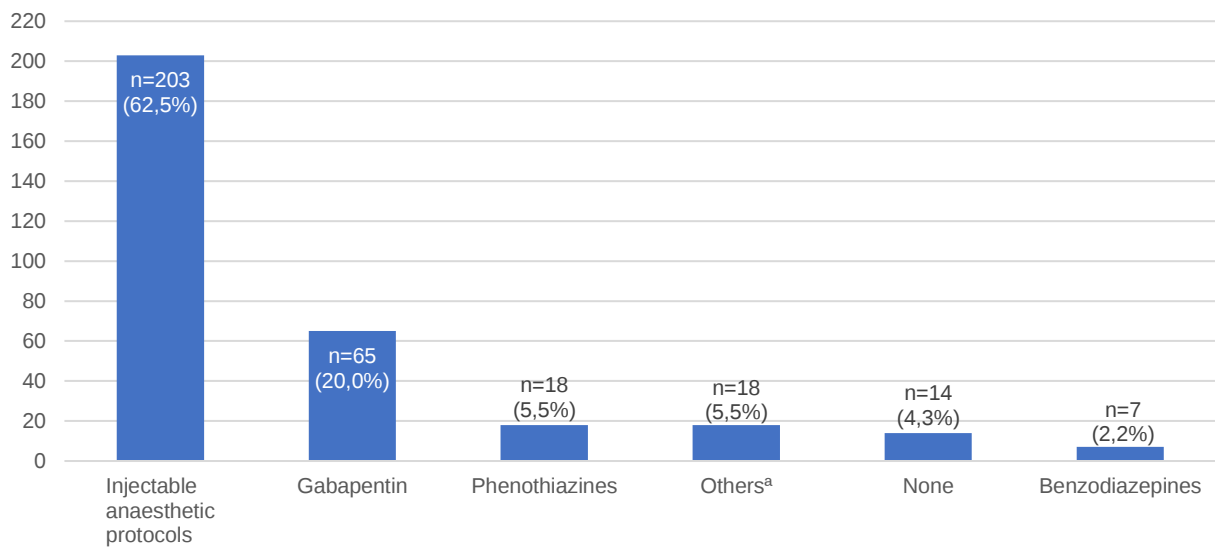


Figure 5. Psychoactive medication choices in cats presenting fractious behaviours.

^a Inhalational anaesthesia and other substances not classified as psychoactive drugs, such as pheromones, were included due to its calming effects.

4. Discussion

This study aimed to evaluate the Portuguese veterinarians' perception of psychoactive drugs by questioning their choices and frequency of use, both generally and in specific situations, as well as identifying some potential misuses in their small animal practice. For those purposes, it sought to explore three hypothesis: a) there is an overall low knowledge about psychopharmacology applied to animal behaviour; b) due to an unawareness of effective psychopharmacological alternatives, Portuguese veterinarians either don't use medication in anxious/fractionous animals, leading to chemical restraints (anaesthetic protocols), or use inadequate physical restraints; c) there is an empirical use of phenothiazines in the presence of an anxious animal because it gives the observer the false perception of an "acute anxiolysis", even though it is known that such molecules should not be used with anxiolytic purposes.

The first hypothesis was supported by the results obtained in this study, since the majority of veterinarians claimed to have knowledge in animal behaviour field and over two-thirds referred to be familiar with the effects of psychoactive drugs. However, approximately the same number of veterinarians referred to ignore the serotonin syndrome, a basic concept in psychopharmacology, and over half of the participants didn't know about the need of a washout period after the administration of psychoactive medication. The second hypothesis was also supported by this study, since the injectable anaesthetic protocols were the first pharmacological choice in the presence of a dog or a cat presenting fractionous behaviours for most veterinarians. The use of phenothiazines was the second choice in dogs and the third in cats in these cases. Also, when presented with acutely stressed dogs, phenothiazines were the second preferable pharmacological approach, only surpassed by dexmedetomidine OTM gel administration, thus partially supporting the third hypothesis. On acutely stressed cats, gabapentin was the veterinarians' main choice, although phenothiazines were also used frequently.

Most veterinarians stated being familiar with psychopharmacology and considered it an asset for pets' welfare. More than half of Portuguese veterinarians receive a fair number of dogs and cats presenting behavioural problems, but prescription rates of psychoactive drugs presented low. Looking into the global prescription of psychoactive drugs, just 28.7% of Portuguese veterinarians prescribe it more than occasionally. According to an old study (Patronek & Dodman, 1999), on behaviour consultations in veterinary small animal practice, "minimal use of drugs for behaviour modification may reflect the limited number of approved drugs, concern about adverse effects or liability for extra label use (...) lack of training regarding the appropriate use of behavioural medication during veterinary education (...)".

Currently there are only five approved psychoactive medications for use in veterinary medicine in Portugal. Their manufacturers and therapeutical indications for behaviour issues are referred in Appendix IV.

Nearly three-quarters of the participants stated they were not lectured psychopharmacology during their veterinary education, supporting the fact that most veterinarians were unacquainted with basic psychopharmacological concepts. Only under one-fifth of veterinarians performed psychoactive polypharmacy, although there are several studies that support the synergistic effect of psychopharmacological combinations (M. E. Gruen & Sherman, 2008; Ogata & Dodman, 2011). The benefits of these combinations are achieved by complementing psychoactive drugs with different speeds of onset and action time. For example, trazodone can be used for its immediate effect, while an SSRI's full effect in the animal is awaited (Ogata et al., 2019; Pineda et al., 2018).

Regarding Portuguese veterinarians that claimed having psychopharmacological knowledge, it was found that benzodiazepines were the most frequently prescribed psychoactive drug (70.54%; n=158), followed by phenothiazines (65.76%; n=146), TCAs (57.44%; n=112) and SSRIs (38.72%; n=95). It is important for owners and veterinarians to be aware that, in the use of benzodiazepines, a potential disinhibitory effect in frightened animals may occur, which could lead to increased aggressiveness when medicated (Dantas & Crowell-Davis, 2019). It was found that drugs with immediate action are largely preferred by this population, suggesting that they are usually not addressing the origin of the maladaptive behaviour, but rather trying to solve the consequence.

Concerning pharmacological tools that help manage acute stressful situations in dogs and cats, it was found that Portuguese veterinarians most frequently use dexmedetomidine OTM gel (22%; n=94) and gabapentin (35.3%; n=112), in dogs and cats respectively. Alpha2-adrenergic agonists (dexmedetomidine OTM gel), benzodiazepines, SARIs (trazodone) and gabapentin all have good anxiolytic properties, which support their use in these situations (Crowell-Davis et al., 2003; Gilbert-Gregory et al., 2016; Korpivaara et al., 2017; van Haaften et al., 2017), with the latter also being used when there is concomitant neuropathic pain (Inkpen, 2015).

When facing threatening situations like fractious behaviours, a preference in injectable anaesthetics was found both in dogs and cats (58,5% and 62,5%, respectively). One of the possible arguments is the lack of bibliography supporting oral medication for fractious behaviours and some even supporting the use of these anaesthetic protocols (Moffat, 2008). Moffat (2008) suggests using a drug combination of butorphanol and medetomidine or dexmedetomidine and midazolam for fractious dogs and cats, as it also provides some anxiolytic activity.

More than one-third of the veterinarians stated that acepromazine is a viable choice regarding behavioural problems and almost half of them considered it to have an anxiolytic activity. In Portuguese veterinary practices, phenothiazines are currently prescribed in dogs and cats presenting acute distress (18,5% and 15,5%, respectively) and fractious behaviours (14,1% and 5,5%, respectively). Acepromazine, a low-potency phenothiazine, is a well-known preanesthetic agents; its additive effects can lower the doses of other combined tranquilizers and potentiate general anaesthesia (Seibert & Crowell-Davis, 2019). It can also help on perioperative pain control (Grint et al., 2010; Hofmeister et al.,

2010) and has anti-emetic properties which can prevent motion sickness during animal transportation, although maropitant citrate might offer a better alternative, since it doesn't have acepromazine's sedative effects (Fatjó, 2013). Acepromazine's anxiolytic properties are minimal. It can be indicated in the management of intense fear responses that require heavy sedation, to prevent self-injury or property damage, but if used as a sole agent, it might increase reactivity to noise and lead to unpredictable behaviour of dogs and cats who are profoundly scared or anxious (Seibert & Crowell-Davis, 2019). According to Overall (2013b), dissociative agents, such as acepromazine, reduce the animal's ability to rationally process environmental stimuli, which is likely to increase rather than decrease the animal's anxious response. For this, acepromazine should never be used as a veterinary behavioural medication.

Portuguese veterinarians also choose to use supplements, nutraceuticals, pheromones or other calming substances and some integrative therapies, such as homeopathy. Some studies evidence that some complementary nutraceuticals and pheromones can have a beneficial effect on the reduction of sound-induced fear, as well as stress and anxiety levels during veterinary consultations (Beata, Beaumont-Graff, Coll, et al., 2007; Beata, Beaumont-Graff, Diaz, et al., 2007; G. M. Landsberg et al., 2015; Pereira et al., 2016). Although they are useful in the management of mild fear and anxiety, in cases of more fearful and potentially dangerous dogs and cats where the sole use of these substances is insufficient, other types of pharmacologic management are indicated (Yin, 2013). Regarding the use of most integrative therapies, such as homeopathy, to the author's knowledge, there are currently no studies that evidence a significant efficacy, so its use in such situations is still questionable.

Finally, this survey-based study faced some limitations. According to information disclosed by the Ordem dos Médicos Veterinários (OMV), there are, at the moment, around 2650 Portuguese small animal practitioners (OMV, 2020). The paucity of data with only 241 Portuguese veterinarians and non-identical response proportions regarding demographical regions make it difficult to determine the representativeness of the evaluated population. The list of officially authorized veterinary practices in Portugal, shared by DGAV, provided a convenient number of practices, but relied on them sharing their details online and including an e-mail address in their profile or website. The survey design also failed to exclude the possibility of repeated responses or guaranteeing that the participant was in fact a veterinarian, as the survey link could have been accessed by multiple personnel (e.g. veterinary students, nurses or other practitioner staff).

5. Conclusions

Research in veterinary behavioural psychopharmacology is still in its early stages. As further psychoactive medication studies in companion animals are published and their effects and results are better understood, veterinarians' options to manage behavioural problems in dogs and cats increase.

Besides that, and to our knowledge, this is the first study evaluating Portuguese veterinarians' perception about the use of psychoactive drugs in the field of clinic veterinary medicine. This study demonstrates the low level of knowledge regarding the use of psychopharmacology in acutely distressed animals, with some anecdotal discrepancies between animal behavioural knowledge and choice of drugs for anxiolysis.

Benzodiazepines, dexmedetomidine OTM gel, gabapentin and trazodone truly present anxiolytic activity, promoting welfare in acute distress states. And they were some of the prescribed drugs in dogs and cats, namely for the visits to the veterinary practices.

But chemical restraint is still one of the techniques used in distressed animals, with higher prevalence in dogs and cats presenting fractious behaviours. Despite acepromazine's beneficial effects in some of the anaesthetic protocols, its misuse alone with the aim to promote calm behaviour is still prevalent between Portuguese veterinarians.

Because of the importance of this area, there is a further need to conduct other studies involving a higher number of Portuguese veterinarians. We hope Portuguese veterinarians take interest in similar projects in the future and that they can implement these findings into their daily veterinary practice. Educational resources that help veterinarians attain more tools to effectively reduce stress and anxiety levels in the dog and cat should also be explored.

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Appendix

Appendix I – List of psychoactive drugs used in dogs for behavioural veterinary medicine.

Drug class	Drug name	Dose in dogs	References
Benzodiazepines (BZDs)	Diazepam	0.55 – 2.2 mg/kg, PO, PRN	(Papich, 2016)
	Alprazolam	0.02 – 0.1 mg/kg, PO, q 8-12h 0.02 mg/kg, PO, PRN (w/ clomipramine)	(Fatjó, 2013) (Crowell-Davis et al., 2003)
Tricyclic Antidepressants (TCAs)	Clomipramine	1 – 3 mg/kg, PO, q 12h	(Papich, 2016)
	Amitriptyline	1 – 2 mg/kg, PO, q 12-24h	(Papich, 2016)
Selective Serotonin Reuptake Inhibitors (SSRIs)	Fluoxetine	Start with 0.5 mg/kg, PO, q 24h, - increase to 1 mg/kg, PO, q 24h	(Papich, 2016)
	Sertraline	2.5 mg/kg, PO, q 24h	(Dodman & Arrington, 2000)
Atypical antidepressants such as: Serotonin Antagonist and Reuptake Inhibitors (SARIs)	Trazodone	2 – 5 mg/kg, PO, q 12h and or bolus (1 hour prior to an anxiety-inducing event)	(M. E. Gruen & Sherman, 2008)
Monoamine Oxidase Inhibitors (MAOIs)	Selegiline	0.5 – 1 mg/kg, PO, q 24h	(Larson & Summers, 2001)
Anticonvulsants	Gabapentin	10 mg/kg, PO, q 8-12h	(Haug, 2008)
Alfa2 agonists	Dexmedetomidine	125 µg/m ² OTM (may re-dose q 2-3h)	(FDA, 2015)

Adapted from Gruen, M., Sherman, B., & Papich, M. (2018). Drugs affecting animal behavior. In J. Riviere & M. Papich (Eds.), *Veterinary Pharmacology and Therapeutics* (10th ed., pp. 416–448). Wiley Blackwell.

Appendix II – List of psychoactive drugs used in cats for behavioural veterinary medicine.

Drug class	Drug name	Dose in cats	References
Benzodiazepines (BZDs)	Diazepam	1 – 4 mg/cat, PO, q 12-24h	(Papich, 2016)
	Alprazolam	0.125 – 0.25 mg/cat, PO, q 12h	(Marder, 1991)
Tricyclic Antidepressants (TCAs)	Clomipramine	1 – 5 mg/cat, PO, q 24h	(Papich, 2016)
	Amitriptyline	5 – 10 mg/cat, PO, q 24h	(Papich, 2016)
Selective Serotonin Reuptake Inhibitors (SSRIs)	Fluoxetine	0.5 – 4 mg/cat, PO, q 24h	(Papich, 2016)
Atypical antidepressants such as: Serotonin Antagonist and Reuptake Inhibitors (SARIs)	Trazodone	50 mg/cat, PO, PRN	(Orlando et al., 2015)
Monoamine Oxidase Inhibitors (MAOIs)	Selegiline	0.5 mg/kg, PO, q 24h	(Papich, 2016)
Anticonvulsants	Gabapentin	20 mg/kg, PO (2-3h prior to an anxiety-inducing event)	(van Haaften et al., 2017)
Alfa2 agonists	Dexmedetomidine	40 µg/kg OTM, IM	(Slingsby et al., 2009)

Adapted from Gruen, M., Sherman, B., & Papich, M. (2018). Drugs affecting animal behavior. In J. Riviere & M. Papich (Eds.), *Veterinary Pharmacology and Therapeutics* (10th ed., pp. 416–448). Wiley Blackwell.

Conhecimento dos Médicos Veterinários Portugueses relativamente à atividade farmacológica e utilização de psicofármacos em Clínica de Animais de Companhia no Cão e no Gato

Este questionário pretende avaliar o nível de conhecimento dos Médicos Veterinários Portugueses que trabalham em Clínica de Animais de Companhia no âmbito da utilização de psicofármacos. Utiliza estas substâncias na actividade clínica diária? Que substâncias ativas usa? Em que situações as utiliza? Considera a psicofarmacologia uma ferramenta válida para a gestão do stress dos animais em ambiente clínico e/ ou hospitalar?

***Obrigatório**

1. Ano de conclusão do curso de Medicina Veterinária? *

A sua resposta _____

2. Em que região do país trabalha e se localiza o seu Centro Médico Veterinário de Atendimento (CAMV)? Se trabalha no estrangeiro, indique qual o país na opção "Outra". *

☐ Norte

☐ Centro

☐ Sul

☐ Madeira

☐ Açores

☐ Outra: _____

3. Atualmente exerce Clínica de Animais de Companhia e especificamente nas espécies cão e/ou gato? *

- ☐ Sim, em ambos
- ☐ Sim, só em cão
- ☐ Sim, só em gato
- ☐ Não
- ☐ Exerci anteriormente

4. Tem conhecimento na área de comportamento animal em cão e/ou gato? *

- ☐ Sim
- ☐ Não

5. Se respondeu "Sim" na pergunta anterior, como qualificaria esse conhecimento?

- | | | | | | | |
|--------------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|---|
| | 1 | 2 | 3 | 4 | 5 | |
| Muito pouco conhecimento | ☐ | ☐ | ☐ | ☐ | ☐ | Excelente conhecimento e muito atualizado |

6. Durante o curso de Medicina Veterinária a utilização de psicofármacos aplicados à intervenção em comportamento de cão e gato foi-lhe lecionada? *

- ☐ Sim
- ☐ Não

7. O CAMV onde trabalha possui algum tipo de distinção habitualmente designada de animal friendly? *

- ☐ Sim
- ☐ Não
- ☐ Não, mas pretende ter num futuro próximo

8. Tem algum Médico Veterinário responsável pela realização de consultas de problemas de comportamento em cão e/ou gato no seu CAMV? *

- ☐ Sim, sou eu
- ☐ Sim, outro colega
- ☐ Não

9. Encontra-se familiarizado com o efeito de psicofármacos (medicação utilizada para alterar o comportamento dos animais)? *

- ☐ Sim
- ☐ Não

10. Com que frequência prescreve psicofármacos? *

- | | | | | | | |
|---------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|--------------------------------|
| | 1 | 2 | 3 | 4 | 5 | |
| Não prescrevo | ☐ | ☐ | ☐ | ☐ | ☐ | Prescrevo com muita frequência |

11. Com que frequência o seu CAMV prescreve psicofármacos? *

	1	2	3	4	5	
Não prescreve	☐	☐	☐	☐	☐	Prescreve com muita frequência

12. Considera que há casos onde a utilização de psicofármacos é uma mais valia para o bem-estar do animal de companhia (cão e/ou gato)? *

- ☐ Sim
- ☐ Não
- ☐ Não sei

13. Encontra-se familiarizado com a utilização de Inibidores Seletivos da Recaptação de Serotonina (SSRI) (ex.: fluoxetina)? *

- ☐ Sim
- ☐ Não

14. Com que frequência prescreve SSRI? *

	1	2	3	4	5	
Não prescrevo	☐	☐	☐	☐	☐	Prescrevo com muita frequência

15. Encontra-se familiarizado com a utilização de Antidepressivos Tricíclicos (TCA) (ex.: clomipramina)? *

- ☐ Sim
- ☐ Não

16. Com que frequência prescreve TCA? *

- | | | | | | | |
|---------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|--------------------------------|
| | 1 | 2 | 3 | 4 | 5 | |
| Não prescrevo | ☐ | ☐ | ☐ | ☐ | ☐ | Prescrevo com muita frequência |

17. Considera as Fenotiazinas (ex.: acepromazina) utilizáveis para problemas de comportamento em animais de companhia? *

- ☐ Sim
- ☐ Sim, mas nunca utilizei
- ☐ Não
- ☐ Não sei

18. Considera que as Fenotiazinas possuem atividade ansiolítica em situações agudas de stress? *

- ☐ Sim
- ☐ Não
- ☐ Não sei

19. Que medicação oral prescreve para reduzir o medo e a ansiedade nos cães em situações agudas (ex.: nas viagens ou fogo de artifício)? Se utiliza outro tipo de medicação, indique qual. *

- ☐ Benzodiazepinas (ex.: diazepam)
- ☐ Fenotiazinas (ex.: acepromazina)
- ☐ Gabapentina
- ☐ Dexmedetomidina gel oral (Sileo®)
- ☐ Antagonistas e Inibidores da Recaptação de Serotonina (SARI) (ex.: trazodona)
- ☐ Não prescrevo nenhuma medicação
- ☐ Outra: _____

20. Que medicação oral prescreve para reduzir o medo e a ansiedade nos gatos em situações agudas (ex.: nas viagens ou fogo de artifício)? Se utiliza outro tipo de medicação, indique qual. *

- ☐ Benzodiazepinas (ex.: alprazolam)
- ☐ Fenotiazinas (ex.: acepromazina)
- ☐ Gabapentina
- ☐ Antagonistas e Inibidores da Recaptação de Serotonina (SARI) (ex.: trazodona)
- ☐ Não prescrevo nenhuma medicação
- ☐ Outra: _____

21. Que medicação utiliza em caso de cães com comportamentos agressivos no CAMV, caso as técnicas de contenção chamadas de animal friendly não resultem? Se utiliza outro tipo de medicação, indique qual. *

- ☐ Protocolos anestésicos injetáveis
- ☐ Benzodiazepinas (ex.: diazepam)
- ☐ Fenotiazinas (ex.: acepromazina)
- ☐ Gabapentina
- ☐ Dexmedetomidina gel oral (Sileo®)
- ☐ Não utilizo nenhuma medicação
- ☐ Outra: _____

22. Que medicação utiliza em caso de gatos com comportamentos agressivos no CAMV, caso as técnicas de contenção chamadas de animal friendly não resultem? Se utiliza outro tipo de medicação, indique qual. *

- ☐ Protocolos anestésicos injetáveis
- ☐ Benzodiazepinas (ex.: alprazolam)
- ☐ Fenotiazinas (ex.: acepromazina)
- ☐ Gabapentina
- ☐ Não utilizo nenhuma medicação
- ☐ Outra: _____

23. Com que frequência recebe em consulta cães com problemas comportamentais (ex.: agressividade, medo, comportamentos compulsivos.) *

	1	2	3	4	5	
Não recebo	☐	☐	☐	☐	☐	Recebo com muita frequência

24. Com que frequência recebe em consulta gatos com problemas comportamentais (ex.: agressividade, medo, comportamentos compulsivos.) *

	1	2	3	4	5	
Não recebo	☐	☐	☐	☐	☐	Recebo com muita frequência

25. Dos seguintes psicofármacos indique os que já utilizou para problemas de comportamento e discrimine a forma de utilização? *

	Não utilizo	Não estou familiarizado com a sua utilização	Utilizo somente em situações pontuais	Utilizo apenas em alguns problemas de comportamento	Utilizo com frequência	É uma das minhas principais escolhas para problemas de comportamento
Benzodiazepinas (ex.: diazepam, alprazolam)	☐	☐	☐	☐	☐	☐
Fenotiazinas (ex.: acepromazina)	☐	☐	☐	☐	☐	☐
Trazodona	☐	☐	☐	☐	☐	☐
Clonidina	☐	☐	☐	☐	☐	☐
SSRI (ex.: fluoxetina)	☐	☐	☐	☐	☐	☐
TCA (ex.: clomipramina)	☐	☐	☐	☐	☐	☐
Inibidores da Monoamina Oxidase IMAO (ex.: selegilina)	☐	☐	☐	☐	☐	☐
Propentofilina	☐	☐	☐	☐	☐	☐
Outros psicofármacos	☐	☐	☐	☐	☐	☐

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26. Se assinalou "Outros psicofármacos" na pergunta anterior, indique qual/quais.

A sua resposta

27. Alguma vez utilizou mais do que um psicofármaco em simultâneo em animais de companhia (cão e/ou gato)? *

☐ Sim

☐ Não

28. Se respondeu "Sim" na pergunta anterior, qual a combinação mais frequentemente utilizada?

A sua resposta

29. Está familiarizado com o conceito de wash out (intervalo entre mudança de diferentes psicofármacos)? *

☐ Sim

☐ Não

30. Está familiarizado com o conceito de síndrome serotoninérgica aplicado à utilização de psicofármacos? *

☐ Sim

☐ Não

Submeter

Appendix IV – List of currently approved psychoactive drugs for behavioural veterinary medicine in Portugal and their summary of product characteristics.

Active substance of psychoactive drug (Commercial name)	Target Species	Pharmaceutical formulation	Therapeutical indication
Acepromazine (VETRANQUIL®)	Dog Cat	Tablet	Tranquilization, sedation and neuro-muscular relaxation: -To facilitate transport. -To reduce agitation, aggression and stress.
Clomipramine (CLOMICALM®)	Dog	Tablet	As an aid in the treatment of separation-related disorders in dogs manifested by destruction and inappropriate elimination (defaecation and urination) and only in combination with behavioural modification techniques.
Dexmedetomidine (SILEO®)	Dog	Oromucosal gel	Alleviation of acute anxiety and fear associated with noise in dogs.
Fluoxetine (RECONCILE®)	Dog	Chewable tablet	As an aid in the treatment of separation-related disorders in dogs manifested by destruction and inappropriate behaviours (vocalisation and inappropriate defaecation and/or urination) and only in combination with behavioural modification techniques.
Imepitoin (PEXION®)	Dog	Tablet	For the reduction of anxiety and fear associated with noise phobia in dogs.

Sources:

Direção Geral de Alimentação e Veterinária (DGAV) (2020) Available at: medvet.dgav.pt. Accessed in: 03/07/2020

European Medicines Agency (EMA) (2020) Available at: ema.europa.eu. Accessed in: 03/07/2020