



# Assessment of a canine Hypersensitivity - Hyperactivity syndrome rating scale

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**Abstract:** Rating scales have been used to evaluate Attention Deficit Hyperactivity Disorder (ADHD) in humans for many years, and ADHD rating scales modified for use in dogs, *canis familiaris*, have been validated and replicated. Still a canine ADHD syndrome has not been well-defined. To date, ADHD rating scales for dog have not been used to address the question of whether dogs with high scores demonstrate behavioural disorders.

In the French model of Zoopsychiatry, Hypersensitivity-Hyperactivity (HSHA) syndrome in dogs has been clinically described and can be considered a potential animal model of human ADHD, as well as a clinically defined canine version of ADHD. This prospective multicentric case study evaluated the usefulness of a translated version of one published ADHD rating scale in studying dogs with HSHA syndrome.

Seventy-eight owners of 78 dogs exhibiting HSHA, diagnosed by veterinary behaviourists filled out a questionnaire. Seventy-eight questionnaires were also administered to owners of healthy dogs that were matched as closely as possible in terms of breed, age, and sex. Four scores were studied: total score, inattention score (IA), and two hyperactivity scores (HI1 and HI2). The accuracy of the different scales in distinguishing HSHA cases from healthy dogs was analysed by Receiver Operating Characteristic (ROC) curves and by calculating the Area Under the ROC Curve (AUC).

The total score ranged from 15 to 46 with a mean of 29.36 in the HSHA group, and from 3 to 29 with a mean of 15.68 in the control group. The AUC for the total score was 0.955 (95% Confidence Interval 0.925-0.984).

This scale had a very good ability to discriminate between dogs with HSHA and healthy matched controls. Determining an appropriate threshold score should help screen for HSHA syndrome in dogs and encourage behavioural consultation.

**Key Words:** ADHD, Behaviour, Diagnosis, Dog, HSHA, Rating scale.

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## Introduction

Human Attention Deficit Hyperactivity Disorder (ADHD) is a disorder that is recognised worldwide (Faraone et al., 2003; Biederman, 2005; Hoogman et al., 2017). ADHD is highly preva-

lent in children (5% to 10%) and can persist into adulthood (Agnew-Blais et al., 2016; Caye et al., 2016). ADHD rating scales have been used for many years for a variety of clinical and research purposes, including screening, determining the effect of treatments, and identifying changes in the condition. Some of these scales have been shown to be useful and valid, as demonstrated by a meta-analysis (Collett et al., 2003). ADHD rating scales (Conners' Rating Scale-Revised (CRS-R) (Conners et al., 1997; 1998), ADHD Rating Scale-IV (ADHDRS-IV) (DuPaul, 1991; 1998; Pappas, 2006)) seem to be effective tools for the initial evaluation of human patients (Collett et al., 2003), and may improve clinical assessment. A French version of the CRS has been validated (Fumeaux et al., 2016). These scales are rated by parents and teachers and provide quantitative measures of symptom severity. A report from Zhang et al. (2005) supports the idea that the ADHD-RS, which is administered by a clinician, can be used to assess ADHD symptom severity. However, even though these scales are part of the diagnostic process, they cannot be considered sufficient.

Domestic dogs are considered to be an interesting genetic and behavioural model for some human psychiatric conditions (Overall, 2000). A dog ADHD rating scale was developed from the Du Paul human questionnaire, which is based on two subscales (Vas et al., 2007). Vas demonstrated the reliability and validity of this scale in assessing attention skills and activity in dogs. This Dog-ADHD-RS for owners has been further used to study the association between *DRD4* gene polymorphisms and activity-impulsivity endophenotypes in German shepherds and Beagles (Hejjas et al., 2007; Kurashi et al., 2013).

These genetic studies echo studies of ADHD in humans. Human ADHD is highly heritable, despite difficulties in identifying candidate genes, which could be responsible for the variance observed in the condition. Evidence is accumulating for an association between some genes (including *DRD4*) and ADHD (Bobb et al., 2006; Wallis et al., 2018). Gene-environment interactions will most likely be the focus of future studies. Vas's Dog-ADHD-RS has also been used to investigate potential non-genetic correlates of the ADHD-like condition in dogs, in association with other questionnaires, not all of which have been validated or published, and an interview questionnaire developed by Hoppe, 2017.

The Vas scale, which was initially developed in Eastern Europe, has been slightly modified (one question was removed because it was not significant) and validated by Lit using online questionnaires in a North American population (Lit et al., 2010). A modified version of the Vas and Lit scales has been used in dogs for metabolite profiling studies in dogs showing ADHD-like behaviours (Puurunen et al., 2016).

To date, the Dog-ADHD-RS has been used to investigate variations in behaviours that are known to be impaired in humans with ADHD, including attention, hyperactivity, and impulsivity (Lit et al., 2010). However, no study has addressed whether dogs with high scores display medical disorders, e.g. a neurological disorder such as hydrocephalus, or demonstrate pathological states related to a behavioural disorder such as an ADHD syndrome. A pathological condition results from behaviours that lose their plasticity, and therefore their adaptive function. In addition, pathological behaviours prevent a return to equilibrium at the end of a behavioral sequence (Pageat, 1998). A variety of terms have been used to describe ADHD in dogs (Campbell, 1973; Luescher, 1993; Overall, 1997; Landsberg, 2003). The diagnosis usually depends on a response to amphetamine or methylphenidate (Luescher, 1993; Piturru, 2014), which French veterinarians are not allowed to prescribe. Thus, the relevance of this diagnostic test has not been evaluated. In addition, there is no consensus on the clinical definition of ADHD in dogs. HSHA syndrome can be considered a clinical description of ADHD syndrome (Marlois, 2001; Pageat cited in Landsberg, 2013), and has been referred to as such in recent publications (Lunõ et al., 2015; Marlois & Beata, 2017; Masson & Gaultier, 2018). HSHA is a positive clinical diagnosis and does not require assessing the response to treatment.

The purpose of the present study was to evaluate the ability of the Lit Dog-ADHD-RS to discriminate between dogs diagnosed with HSHA according to the French definition and healthy

matched controls. If this scale effectively distinguishes between the two groups, then establishing a cut-off value may be helpful for screening individual animals for HSHA.

## Materials and methods

This study was conducted and reported according to established STARD (Standards for Reporting of Diagnostic Accuracy Studies) guidelines (Bossuyt et al., 2015).

### *Study design*

ZOOPSY (French Association of Veterinary Psychiatry)'s members received an email inviting them to participate in this prospective study. The translated questionnaire was sent to those who accepted. Survey data were collected between June 2017 and February 2018. At the end of a behavioural consultation, when a dog was diagnosed HSHA according to Pageat's criteria (Pageat, 1998), modified (Mege et al., 2003) as shown in Table 1, the owner was asked to fill out the questionnaire. Owners of paired control dogs completed the same questionnaire.

### *Participants*

Sixteen French veterinarians from different French regions and one Belgian veterinarian, all ZOOPSY members, participated in the study. Dogs eligible for inclusion went through a behavioural consultation and presented a positive clinical HSHA diagnosis according to the criteria presented in Table 1. The study did not involve additional handling or discomfort for the dogs. Dogs with comorbidities were excluded if ADHD syndrome was not the predominant problem. Dogs under treatment were also excluded. The veterinarians selected the dogs when the owners and themselves had time to apply the protocol. Eligible dogs formed a convenience sample of eighty-five dogs with a diagnosis of HSHA. The breed, age, sex, and reproductive status were recorded. No personal information about the owners has been recorded.

Seven dogs were not included in the study because matched controls could not be found for them during the study period, mostly due to their morphotype. Thus, 78 dogs were finally included in the study.

Seventy-eight paired control dogs were recruited through veterinary practices and email groups for canicross or bikejoring. The control dogs were matched one-on-one to the HSHA dogs as closely as possible, in terms of breed (including cross breeds), age, and, if possible, sex and reproductive status. They all went through a clinical examination by five of the participating veterinarians. They had to be in good physical and mental health. These dogs did not explicitly meet the criteria for HSHA, which did not mean they had to be calm. They could not be under treatment with any medication that may have changed behaviour, including dietary supplements.

Lifestyle (e.g. apartment or house), specific activities, and training courses were not taken into consideration for any of the groups. However, physiological requirements and behavioral needs had to be fulfilled to allow inclusion.

### *Test methods*

The reference is the clinical diagnosis of HSHA, for which the symptoms are pre-specified (Table 1). These criteria are taught in the French school of Zoopsychiatry and are thus shared by the veterinarians who participated in this study, all of whom are members of ZOOPSY. In other countries a reference test assessing the response to stimulants related to the diagnosis of dog ADHD could be used, though this type of test should undergo validation studies.

**Table 1:** Criteria used to establish a diagnosis of canine HSHA

Signs must have been present since an early age. The signs are not explained by the presence of other diseases. Physiological and behavioral needs are fulfilled. The dog exhibits:
<ul style="list-style-type: none"> <li>- Lack of or delay in acquiring bite control in a puppy over 2 months of age</li> <li>- Inability to stop a behavioural sequence or immediate start of a new one</li> <li>- Hypersensitivity associated with a behavioural sequence in reaction to any stimulus, even to those that are continuously present in the dog's environment</li> </ul>

#### ADHD rating scale

The questionnaire used in this study was from Lit et al. (2010) (Table 2) translated into French.

**Table 2:** ADHD rating scale for dogs' items (Lit et al., 2010)

	Never/ Rarely 0	Occasionally 1	Often 2	Very Frequently 3	Always 4
1. Other things attract attention					
2. Loses interest easily					
3. Difficulty concentrating					
4. Difficulty maintaining stay					
5. Barks endlessly					
6. Fidgets or in constant motion					
7. Doesn't pay attention to someone speaking to him/her					
8. Likes active play/running around					
9. Difficulty performing practiced tasks					
10. Reacts hastily/anticipates					
11. Easily distracted					
12. Cannot wait					

The scale was translated into French by the author, then translated back into English by an English teacher who had not seen the original English version and sent to Lit, who validated the back-translation. This methodology was intended to approximate recommendations for transcultural translation of a questionnaire (Beaten et al., 2000).

The scale includes 12 items, scored as follows: 0 (Never/ Rarely), 1 (Occasionally), 2 (Often), 3 (Very Frequently), or 4 (Always). A global score is calculated for each dog, as well as a score for each of the three subscales: the inattention subscale (IA, questions 1, 2, 3, 7, 9, and 11), the hyperactivity-impulsivity subscale 1 (HI1, questions 4, 5, 6, and 12), and the hyperactivity-impulsivity subscale 2 (HI2, questions 6, 8, and 10). According to Lit, the HI2 scale is not affected by training status, unlike the two other subscales (Lit et al., 2010). This scale has not been validated for diagnostic use and a positive cut-off for this scale has not been established. We attempted to explore the value of various thresholds after the data were analysed.

Participating veterinarians were aware of the clinical diagnosis before having the questionnaire completed by the owner since they asked the questions at the end of the consultation.

#### Statistical analysis

Quantitative variables are shown as means and standard deviations, and qualitative variables as counts and percentages. The four scores for the different scales (Total, IA, HI1, HI2) were studied in each group. A Box-and-Whisker plot was used to depict the two groups.

The overall ability of the different scales to distinguish HSHA cases from control dogs was analysed by ROC curves.

A ROC curve is a plot of the sensitivity (proportion of HSHA dogs with a score above a thresh-

old (true positive (TP) among dogs with HSHA (TP + false negatives (FN)) versus 1-specificity (proportion of control dogs with a score below a threshold (true negatives (TN) among control dogs (false positives (FP) + TN)) over all possible threshold values for the score (Greiner et al., 2000). The area under the ROC curve (AUC) is an overall measure of how well a parameter can distinguish between the HSHA dogs and the control dogs. If the two groups were perfectly separated with no overlap, the AUC would equal 1. An AUC of 0.5 indicates no difference between the two distributions, meaning the test is not suitable for that purpose.

The AUCs were used to select the score with the best overall diagnostic ability. AUCs were compared between scores using the DeLong test, a non-parametric test for comparison of AUCs.

Sensitivity, specificity, positive predictive value (PPV, probability that a dog has HSHA if its score is above the threshold, so if its test is positive), and negative predictive value (NPV, probability that a dog is not HSHA if its score is below the threshold, so if its test is negative) were calculated for different thresholds. The predictive value of any diagnostic test is strongly influenced by the prevalence of the condition in the population. It is what connects the validity of the test, as determined by sensitivity and specificity, with condition in the reality. Currently, the prevalence of HSHA in French dogs is not known. Therefore, it is only possible to make assumptions. We calculated the PPV and NPV for three hypothetical prevalence rates: 1.5%, 5.6%, and 16.6% (Table 7). The 1.5% rate is based on the estimates of veterinarians participating in the study who also have a generalist practice (estimates ranged from 1.5% to 7.5%). The 5.6% rate is the estimated rate of ADHD prevalence in children in France (Haute Autorité de Santé, 2014). This human rate can be as high as 16.6%, depending on the diagnostic method used (Haute Autorité de Santé, 2014), so 16.6% was selected as the highest potential rate for our projections.

PPV and NPV were calculated using the Bayes theorem, from sensitivity, specificity, and the assumed prevalence of HSHA.

Statistical analyses were performed using R software, version 3.4.3. P-values of less than 0.05 were considered significant.

## Results

The raw data of the scores are available in Supplementary file 2.

### *Description of the study population*

Table 3 summarizes the characteristics of the study population.

The sex ratio (SR) in the HSHA group is 1.69 and 1.29 in the control group.

**Table 3.** Description of the two groups

Group	HSHA N = 78	Control N = 78	Total N = 156
Sex			
Female	29 (37.2%)	34 (43.6%)	63 (40.4%)
Male	49 (62.8%)	44 (56.4%)	93 (59.6%)
N	78	78	156
Reproductive status			
Non-Neutered	43 (55.1%)	52 (66.7%)	95 (60.9%)
Neutered	35 (44.9%)	26 (33.3%)	61 (39.1%)
N	78	78	156
Weight in kg			
Mean (SD)	23.04 (11.1)	23.20 (10.6)	23.12 (10.8)

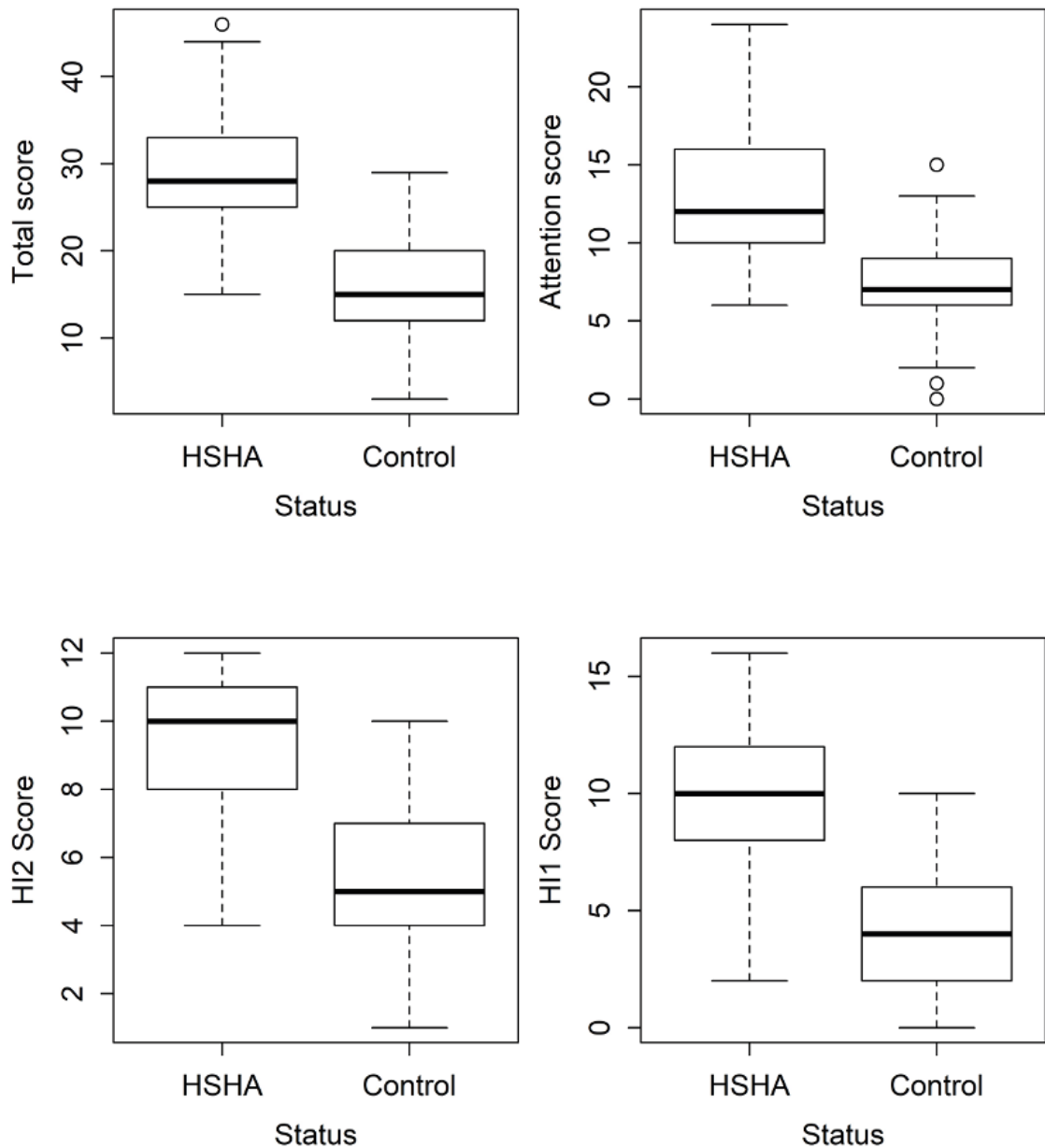
Group	HSHA N = 78	Control N = 78	Total N = 156
N	78	78	156
Age in years			
Mean (SD)	1.7 (1.33)	1.80 (1.50)	1.7 (1.4)
N	78	78	156

### Description of the scores

The scores for each group are shown in Table 4 and displayed in the Box-and-Whisker plot (Fig. 1). The mean of the total score was higher in the HSHA group (29.36) than in the control group (15.68), of a possible maximum score of 48. This pattern was also true for all of the subscale scores, but the greatest difference was observed in the total score.

**Table 4:** Description of the scores by group – (mean (SD), Median, Q1-Q3, Min-Max)

Score	HSHA N = 78	Control N = 78	Total N = 156
<b>Total Score</b>			
Mean (SD) Median	29.36 (6.64)	15.68 (5.26)	22.52 (9.10)
Q1-Q3	28.00	15.00	22.00
Min-Max	25-32.75	12.00-19.75	15.00-28.25
	15.00-46.00	3.00-29.00	3.00-46
<b>IA Score</b>			
Mean (SD)	13.37 (4.14)	7.51 (2.76)	10.44 (4.58)
Median	12.00	7.00	10.00
Q1-Q3	10.25-16.00	6.00-9.00	7.00-13.00
Min-Max	6.00-24.00	0.00-15.00	0.00-24.00
<b>HI1 Score</b>			
Mean (SD)	9.85 (3.18)	3.91 (2.40)	6.88 (4.09)
Median	10.00	4.00	7.00
Q1-Q3	8.00-12.00	2.00-5.75	3.00-10.00
Min-Max	2.00-16.00	0.00-10.00	0.00-16.00
<b>HI2 Score</b>			
Mean (SD)	9.18 (2.12)	5.28 (2.28)	7.23 (2.94)
Median	10.00	5.00	7.00
Q1-Q3	8.00-11.00	4.00-7.00	5.00-10.00
Min-Max	4.00-12.00	1.00-10.00	1.00-12.00

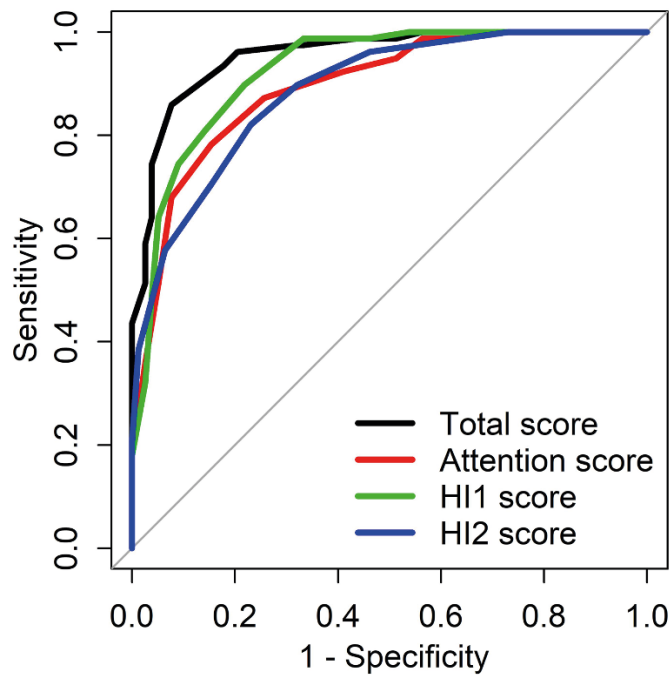


**Figure 1.** Representation of the total score and subscale scores in the two groups

The central box spans the first quartile to the third quartile (interquartile range, IQR), which was 25-32.75 and 12-19.75 for the HSHA and control groups, respectively. The IQRs of the two populations were both equal to 7.75. The horizontal line inside the box shows the median for each group (28 and 15, respectively). The upper whisker extends from Q3 to the highest score within the range defined by  $Q3 + 1.5 * IQR$  ( $32.75 + (1.5 * 7.75)$ ). The lower whisker extends from Q1 to the lowest score within the range defined by  $Q1 - (1.5 * 7.75)$ . Empty circles represent extreme values, which means data points outside of the whisker thresholds but within the range defined by  $3 * IQR$ . There was only one outlying data point for the HSHA total score, while there were three for the Attention score in the control group, which is totally consistent with the variability within the sample groups.

### ROC curve analysis

The ROC curves for the total score and for the three subscale scores are presented in Figure 2, and the AUCs are displayed in Table 5.



**Figure 2.** The four ROC curves corresponding to the four scores: Total, IA, HI1, HI2

The ROC curve is the plot of the sensitivity ( $TP / (TP+FN)$ ) versus 1-specificity ( $1-(TN / (FP+TN))$ ) over all possible threshold values for the score (Table 6)

**Table 5:** Area under the ROC curve (AUC) for each score

Score	AUC	95% CI
Total Score	0.955*	[0.925, 0.984]
IA Score	0.893	[0.844, 0.941]
HI1 Score	0.924	[0.884, 0.965]
HI2 Score	0.886	[0.837, 0.935]

The AUC for the total score was statistically (\*) higher than the AUCs for each subscale score (DeLong test,  $p$ -values: 0.002, 0.025, and 0.01)

The three subscale scores had a good ability to discriminate between healthy or HSHA dogs (AUC above 0.85), and the total score had a very high AUC (0.952), with good precision for each estimate (narrow confidence interval). The AUC for the total score was statistically higher (\*) than the AUCs for each subscale score ( $p$ -values: 0.002, 0.025, and 0.01).

This scale shows a very good ability to discriminate between dogs with HSHA and healthy matched controls in the study population.

The sensitivity and specificity associated with the different possible threshold values for the total score are displayed in Table 6.



**Table 6:** Sensitivity, specificity, [95% confidence intervals] for various total score thresholds

Threshold	Sensitivity [95% CI]	Specificity [95% CI]
3	1.000 [0.954, 1.000]	0.013 [0.000, 0.069]
4	1.000 [0.954, 1.000]	0.026 [0.003, 0.090]
7	1.000 [0.954, 1.000]	0.051 [0.014, 0.126]
8	1.000 [0.954, 1.000]	0.090 [0.037, 0.176]
9	1.000 [0.954, 1.000]	0.115 [0.054, 0.208]
10	1.000 [0.954, 1.000]	0.167 [0.092, 0.268]
12	1.000 [0.954, 1.000]	0.282 [0.186, 0.395]
13	1.000 [0.954, 1.000]	0.359 [0.253, 0.476]
14	1.000 [0.954, 1.000]	0.436 [0.324, 0.553]
15	0.974 [0.910, 0.997]	0.513 [0.397, 0.628]
16	0.974 [0.910, 0.997]	0.590 [0.473, 0.700]
17	0.962 [0.892, 0.992]	0.641 [0.524, 0.747]
18	0.962 [0.892, 0.992]	0.718 [0.605, 0.814]
19	0.962 [0.892, 0.992]	0.744 [0.632, 0.836]
20	0.949 [0.874, 0.986]	0.782 [0.674, 0.868]
21	0.923 [0.840, 0.971]	0.859 [0.762, 0.927]
22	0.872 [0.777, 0.937]	0.897 [0.808, 0.955]
23	0.821 [0.717, 0.898]	0.936 [0.857, 0.979]
24	0.795 [0.688, 0.878]	0.962 [0.892, 0.992]
25	0.679 [0.564, 0.781]	0.974 [0.910, 0.997]
26	0.667 [0.551, 0.769]	0.974 [0.910, 0.997]
27	0.564 [0.447, 0.676]	0.987 [0.931, 1.000]
28	0.487 [0.372, 0.603]	0.987 [0.931, 1.000]
29	0.436 [0.324, 0.553]	1.000 [0.954, 1.000]
30	0.397 [0.288, 0.515]	1.000 [0.954, 1.000]
31	0.333 [0.231, 0.449]	1.000 [0.954, 1.000]
32	0.256 [0.164, 0.368]	1.000 [0.954, 1.000]
33	0.231 [0.143, 0.340]	1.000 [0.954, 1.000]
34	0.218 [0.132, 0.326]	1.000 [0.954, 1.000]
35	0.179 [0.102, 0.283]	1.000 [0.954, 1.000]
36	0.128 [0.063, 0.223]	1.000 [0.954, 1.000]
38	0.115 [0.054, 0.208]	1.000 [0.954, 1.000]
39	0.103 [0.045, 0.192]	1.000 [0.954, 1.000]
40	0.077 [0.029, 0.160]	1.000 [0.954, 1.000]
41	0.064 [0.021, 0.143]	1.000 [0.954, 1.000]
42	0.038 [0.008, 0.108]	1.000 [0.954, 1.000]
44	0.013 [0.000, 0.069]	1.000 [0.954, 1.000]

The PPVs and the NPVs based on various hypothetical prevalence of HSHA are displayed in Table 7.

**Table 7:** Positive predictive value (PPV) and negative predictive value (NPV) for various total score thresholds for an estimated prevalence of 1.5%, 5.6%, or 16.6%

Threshold	Specificity	Sensitivity	PPV (1.5%)	NPV	PPV 5.6%)	NPV	PPV 16.6%	NPV
14	0.436	1.000	0.026	1.000	0.090	1.000	0.261	1.000
15	0.513	0.974	0.030	0.999	0.101	0.997	0.285	0.990
16	0.590	0.974	0.035	0.999	0.117	0.998	0.321	0.991
17	0.641	0.962	0.039	0.999	0.130	0.997	0.348	0.988

Threshold	Specificity	Sensitivity	PPV (1.5%)	NPV	PPV 5.6%)	NPV	PPV 16.6%	NPV
18	0.718	0.962	0.049	0.999	0.160	0.997	0.404	0.989
19	0.744	0.962	0.054	0.999	0.173	0.997	0.427	0.990
20	0.782	0.949	0.062	0.999	0.196	0.996	0.464	0.987
21	0.859	0.923	0.091	0.999	0.268	0.995	0.566	0.982
22	0.897	0.872	0.115	0.998	0.322	0.992	0.629	0.972
23	0.936	0.821	0.163	0.997	0.417	0.989	0.718	0.963
24	0.962	0.795	0.239	0.997	0.536	0.988	0.804	0.959
25	0.974	0.679	0.288	0.995	0.597	0.982	0.841	0.939
26	0.974	0.667	0.284	0.995	0.593	0.981	0.838	0.936
27	0.987	0.564	0.401	0.993	0.711	0.976	0.898	0.919
28	0.987	0.487	0.367	0.992	0.680	0.972	0.883	0.906
29	1.000	0.436	1.000	0.991	1.000	0.969	1.000	0.899

The higher the threshold, the better the specificity, meaning that all control dogs will score under the threshold. However, the sensitivity weakens as the threshold increases, which means that the rate of false negatives will be higher.

In these matched, case-control population groups, considering a prevalence of 1,5%, the probability of a dog having HSHA is 1.00 if the score is  $\geq 29$ . The proportion of actually affected dogs among dogs that tested negative with a cut-off of 29 is 0.009 (1-NPV). The proportion of actually non-affected dogs among the positives is 0.00.

The probability of a dog not being affected with a score of 14 or lower is 1.00. At this threshold the proportion of affected dogs that score negative is 0.00, but the proportion of actually non-affected dogs that score positive is 0.97 (1-PPV).

## Discussion

This study was conducted by French speaking veterinarians in France and Belgium. The results could be different in another country, especially since there is no consensus on the clinical definition of ADHD in dogs. A large number of veterinarians were involved in diagnosing the condition so, the diagnostic criteria may not have been applied consistently, though these vets follow the same definition of HSHA. Some veterinarians reported occasional difficulties in the interpretation of some questionnaire items by the owners. Some items would probably benefit from being reformulated or explained in more detail as they were in the original questionnaires to be clearer for a French population. For example, item 5 "Barks endlessly" would benefit from being clarified, potentially by adding: "in response to seemingly unimportant things".

Fewer veterinarians were responsible for recruiting the controls and could have created a bias by choosing very calm dogs to serve as controls. It was difficult to find dogs that matched the required criteria (breed, age, sex, reproductive status) during the study period. It is unlikely that this potential bias had a large effect all the more since some of the control cases display high scores.

There were more males in the HSHA group than in the control group (the sex ratios were 1.69 and 1.29, respectively). There were more neutered individuals in the HSHA group. These differences may be due to many factors, primarily the difficulty of finding very closely matched dogs. The results reported here cannot provide information about the prevalence of clinical ADHD in different sex, weight, and age groups, since this was not an epidemiological study; our population may not be representative of all dogs with HSHA. It is possible that dogs with HSHA are sterilized more often than other dogs in the hopes of making them calmer. Lit et al. (2010) showed that the

variables age, breed group and training status accounted for very little variance in the subscales scores. The subscale scores were not affected by sex when controlling for age (Lit et al., 2010).

There was no statistically significant difference in the diagnostic performance of the questionnaire to discriminate HSHA from control with respect to sex, age, or weight (comparison of the total score AUC by DeLong test,  $p$ -values: 0.583, 0.924, and 0.735, respectively; supplementary file 3). Given the small sample size, the dogs were divided into two balanced groups for the parameters age and weight. The influence of these factors on the different scores were not considered in this study.

The results confirm the usefulness of the scale and support the hypothesis that dogs with high scores should be considered to have a pathological condition, and potentially to have HSHA as defined by the clinical criteria used in this study. These dogs need medical care with specialized oversight.

The choice of a cut-off rate depends on the medical and prevention strategy. Using a score of 29 and above, we are almost sure to identify only dogs with HSHA. If the prevalence turns out to be much higher, this threshold could drop. Below a threshold of 14, a dog is unlikely to have HSHA. A prevalence within a range of 1.5% to 16.6% seems to have little effect on the choice of the proposed cut-off rates. There is uncertainty regarding the thresholds that were proposed, and they should be confirmed in another study. It is essential to explore the prevalence of HSHA in the canine population.

This scale should not be considered as a replacement tool for clinical diagnosis but as a useful tool to screen HSHA in dogs. Especially it could be used by canine professionals who are not veterinary behaviourists. It could be used in behavioural medicine to launch searches to specify HSHA if necessary as well as to evaluate medication and behaviour-modification techniques used. Further studies are needed to evaluate the relevance of this tool in the context of differential diagnosis, since in this study the controls did not exhibit any pathology. Potential comorbidities should also be considered.

## Conclusions

The dog ADHD-RS (Lit et al., 2010) seems to be a very promising questionnaire tool for discriminating between dogs with and without HSHA which may be useful for research and clinical diagnosis. Further studies considering other behavioural diagnosis as well as studies in a population where prevalence is known are needed to validate clinical thresholds.

An initial working hypothesis is that a score of 29 or more should lead to a behavioral consultation. For a score between 24 and 29, a behavioral consultation is highly recommended. For a score between 14 and 24, behavioral modifications alone or a training program can be put in place along with a close monitoring, whereas for scores under 14 it is quite unlikely that the dog has HSHA; although this does not exclude a potential need for behavioural management.

Similar to other scales (Collett et al., 2003), the ADHD-RS should not be used as the sole evaluation tool. A complete behavioural assessment must be carried out, including a differential diagnosis.

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## Author contributions

N. Marlois, C. Béata, and M. Marion conceived the idea for the study.

N. Marlois, D. Groux, F. Subtil, C. Mege, C. Béata, and G. Sarcey designed the study.

N. Marlois, D. Groux, C. Mege, N. Massal, S. Masson, and M. Marion conducted the experiments.

F. Subtil, N. Marlois, D. Groux, C. Mege, G. Sarcey, and S. Masson analysed and interpreted the data.

N. Marlois, D. Groux, wrote the draft, F. Subtil, C. Mege, C. Béata, G. Sarcey, N. Massal, S. Masson, M. Marion and N. Marlois provided proofreading and revision.

All authors discussed the results and commented on the manuscript, they all approved the version to be submitted.

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### Realizzazione di una scala di valutazione della sindrome da ipersensibilità-iperattività canina

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### Sintesi

Per molti anni le scale di valutazione sono state utilizzate per valutare il disturbo da deficit di attenzione e iperattività (ADHD) negli esseri umani e, modificate per l'uso nei cani, sono state convalidate e replicate. Ancora oggi non esiste una definizione precisa della sindrome canina ADHD e le scale di valutazione dell'ADHD per cani non sono state utilizzate per verificare se i cani con punteggi elevati mostrino disturbi comportamentali.

Nel modello francese di zoopsichiatria, la sindrome da ipersensibilità-iperattività (HSHA) nei cani è stata clinicamente descritta e può essere considerata un potenziale modello animale di ADHD umano, nonché una versione canina clinicamente definita dell'ADHD. Questo studio multicentrico prospettico ha valutato l'utilità di una versione tradotta di una scala di valutazione dell'ADHD nello studio dei cani con sindrome HSHA.

Settantotto proprietari di 78 cani che esibivano HSHA, diagnosticata da veterinari esperti in comportamento, hanno compilato un questionario. Settantotto questionari sono stati somministrati anche a proprietari di cani sani che sono stati abbinati in termini di razza, età e sesso. Sono stati studiati quattro punteggi: punteggio totale, punteggio di disattenzione (IA) e due punteggi di iperattività (HI1 e HI2). L'accuratezza delle diverse scale nel distinguere i casi di HSHA dai cani sani è stata analizzata mediante le curve ROC (Receiver Operating Characteristic) e calcolando l'area sotto la curva ROC (AUC).

Il questionario ADHD-RS per il cane sembra essere uno strumento questionario molto promettente per discriminare tra cani con e senza HSHA e può essere utile per la ricerca e la diagnosi clinica. Per convalidare le soglie cliniche sono necessari ulteriori studi che considerino altre diagnosi comportamentali, nonché studi in una popolazione di cui è nota la prevalenza.

Una prima ipotesi di lavoro è che un punteggio di 29 o superiore dovrebbe portare a una consultazione comportamentale. Per un punteggio compreso tra 24 e 29, è altamente raccomandata una consulenza comportamentale. Per un punteggio compreso tra 14 e 24 si possono mettere in atto modificazioni comportamentali da sole o un programma di rieducazione insieme ad un attento monitoraggio, mentre per punteggi inferiori a 14 è abbastanza improbabile che il cane abbia HSHA; sebbene ciò non escluda una potenziale necessità di gestione comportamentale.

Analogamente ad altre scale, l'ADHD-RS non dovrebbe essere utilizzato come unico strumento di valutazione. Deve essere eseguita una valutazione comportamentale completa, inclusa una diagnosi differenziale.