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# Questionnaire-based behaviour analysis of Cavalier King Charles spaniels with neuropathic pain due to Chiari-like malformation and syringomyelia

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ABSTRACT

Chiari-like malformation (CM)/syringomyelia (SM) is a disease complex recognised in Cavalier King Charles spaniels (CKCSs) that can lead to neuropathic pain (NeP). In humans, NeP is associated with anxiety, depression and reduced quality of life (QoL). In this study, databases of three specialist veterinary centres were searched and CKCS breed societies and health forums were contacted to identify CKCS with an imaging diagnosis of CM/SM. Owners completed questionnaires on behaviour, signalment, general health status, NeP and QoL. Data were analysed from 122 dogs out of 564 questionnaires completed, after incomplete questionnaires and data from dogs that had other potentially debilitating disease processes were excluded. NeP severity score was significantly and positively correlated with 'stranger-directed' fear ($r_S = 0.28$), non-social fear ($r_S = 0.34$), 'separation-related' behaviour ($r_S = 0.38$), attachment behaviour ($r_S = 0.24$), excitability ($r_S = 0.21$) and proxy for pain sensation ($r_S = 0.29$). Increased NeP was also significantly associated with decreased QoL ($r_S = 0.47$), ability to settle ($r_S = 0.26$) and willingness to exercise ($r_S = 0.50$). Severity of NeP was positively associated with certain fear-associated behaviour and with decreased owner-perceived QoL. Thus, neurobehavioural changes should be considered in the management of NeP in CKCS with CM/SM.

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## Introduction

An estimated 95% of Cavalier King Charles spaniels (CKCSs) are affected by Chiari-like malformation (CM) and around 70% develop syringomyelia (SM) (Dewey and Rusbridge, 2008; Parker et al., 2011). In humans, Chiari-type I malformation (the human counterpart to CM) and SM are associated with neuropathic pain (NeP) and present with a variety of symptoms, including headaches, pain in the trigeminal territory, back pain, temporomandibular joint pain and spontaneous pain (Todor et al., 2000; Thimineur et al., 2002). NeP is defined as pain arising as a direct consequence of a lesion or disease process which affects the somatosensory system (Grubb, 2010). The resulting abnormal somatosensory processing can manifest as (1) dysaesthesia, a spontaneous or evoked unpleasant abnormal sensation (people with this condition describe burning-type pain, pins and needles and other strange sensations); (2) allodynia, pain from a stimulus which is not normally painful, such as light touch or motion; (3) hyperpathia, increased pain from stimuli which are normally painful; or (4) causalgia, a constant, burning-type pain (Gilron et al., 2006; Rusbridge and Jeffery, 2008).

CM/SM in CKCS is commonly associated with pain, especially in the cervical region, and with neurological dysfunction, e.g. scoliosis, limb paresis and ataxia (Rusbridge et al., 2000, 2006). Affected dogs might be hypersensitive to touch and often scratch an area on the shoulder, ear, neck or sternum, commonly only on one side of the body without making skin contact, so called phantom scratching (Rusbridge et al., 2006). Some dogs perform facial or head rubbing or spontaneous vocalisations. Such clinical signs are thought to indicate the presence of the animal's perception of NeP, possibly due to damage of the spinal dorsal horn grey matter secondary to SM, as well as overcrowding of the foramen magnum and subsequent compression of the trigeminal nuclei in the caudal brainstem (Todor et al., 2000; Rusbridge et al., 2006; Rusbridge and Jeffery, 2008).

Maximal syrinx width, length and asymmetry strongly predict signs of pain, whilst the degree of cerebellar herniation does not (Lu et al., 2003; Rusbridge et al., 2007; Cerda-Gonzalez et al., 2009). The dorsal horn of the spinal grey matter is central for processing and transmission of sensory information to the brain.

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Neural connections in the dorsal horn are 'plastic' and therefore can be re-organised, which can result in persistent pain (Stanfa and Dickenson, 2004).

In human and veterinary medicine, NeP is problematic due to its severity, chronic nature and resistance to simple analgesics (Gilron et al., 2006; Grubb, 2010). In people with NeP, neurobehavioural co-morbidities and cognitive impairment are common; as a consequence, cognitive and behavioural interventions play a growing role in the successful management of NeP (Gilron et al., 2006). Around one third of people with NeP report having neurobehavioural disorders, such as depression and anxiety (Gustorff et al., 2008) and it is important to consider the possibility that dogs with NeP may also have neurobehavioural co-morbidities. Furthermore, in humans, NeP is thought to have an even greater impact on the quality of life (QoL) than other chronic pain conditions (Grubb, 2010). The aim of this study was to investigate the impact of NeP associated with CM/SM on the behaviour and QoL of affected CKCS. CM/SM is currently the best characterised NeP condition in dogs and therefore was used for this questionnaire-based study.

## Materials and methods

### Animals

CKCS were selected by searching the databases of the authors' referral hospitals for CKCS with a diagnosis of CM/SM made by a board-certified neurologist, based on magnetic resonance imaging (MRI) of the brain and cervical spinal cord, from January 2004 to March 2010. The owners of these CKCS were contacted by letter and asked to complete an on-line questionnaire. Additionally, owners of CKCS with an imaging diagnosis of CM/SM were invited to participate in the study through CKCS breed societies and health forums in the USA, UK and the Netherlands. The web-based questionnaire was restricted to one questionnaire per Internet protocol (IP) address and was password protected. The results were anonymised and confidential. The study was approved by the Royal Veterinary College Institutional Animal Care and Ethics Committee (approval number 20101006).

### Procedure and data collection

A questionnaire was designed using previously validated questionnaires to assess health related QoL in dogs with chronic illness, such as heart diseases (Freeman et al., 2005) or chronic pain due to degenerative joint disease (Wiseman-Orr et al., 2006) and to assess behavioural changes in dogs which might be associated with NeP (Hsu and Serpell, 2003). The questionnaire consisted of three main sections.

#### Section 1

This section collected demographic information, including country of residence, breed, sex, age and information relating to general health and medication status, including a range of conditions which might affect perception of pain or discomfort and confound data, such as a former diagnosed skin condition, non-compensated heart condition, seizures, otitis media with effusion, 'fly-catching' behaviour, arthritis or intervertebral disc disease. Importantly, this section included specific information on the CM/SM status of the individual dog, including the date of MRI to confirm a suspected CM/SM diagnosis and its current treatment, if any.

#### Section 2

Questions asked in this section aimed to provide an insight into the dog's general behaviour, any clinical manifestations of CM/SM and owner perceived QoL. Respondents were asked to what degree they had observed the following NeP signs of CM/SM in their dog on a semantic 5-point differential-type rating scale (Oosgood et al., 1957; Hsu and Serpell, 2003: behaviour is exhibited 0 = never, 1 = seldom, 2 = sometimes, 3 = usually, 4 = always): (1) persistent, compulsive scratching with no underlying skin disease; (2) facial rubbing; (3) hypersensitivity to touch; (4) unexplained yelping; (5) reluctance to lift head; (6) reluctance to bend neck to eat; or (7) reluctance or pain when defaecating. Scores were averaged across these clinical signs to determine an individual NeP severity score (NeP score). The same scale was also used to establish a locomotory score and a score for sleeping/resting. To quantify owner perceived QoL, owners were asked to rate their dog's overall QoL on a fixed scale as follows: 1 = could not be better; 2 = good; 3 = fairly good; 4 = neither good nor bad, 5 = fairly poor; 6 = poor; 7 = could not be worse or 8 = do not know.

#### Section 3

This section was based on a questionnaire to evaluate behaviour, previously validated using 203 dogs with known behavioral anomalies and 1851 control dogs (Hsu and Serpell, 2003). This section had 11 broad categories: 'stranger-directed' aggression; 'owner-directed' aggression; 'stranger-directed' fear; non-social fear; 'dog-directed' fear; 'separation-related' behaviour; attachment or attention seeking behaviour; trainability; chasing behaviour; excitability; and pain sensitivity. The aforementioned sliding scale from 0 to 4 was used to quantify responses. The loading factors for each question established by Hsu and Serpell (2003) were used for analysis of each behaviour category.

### Criteria for inclusion and exclusion

CKCS were only included in further analysis if the dog was >1 year of age, alive at the time of questionnaire entry and had a stated date of an MRI that had confirmed a diagnosis of CM/SM. CKCS were excluded from the study if they had been diagnosed with one of the following conditions or clinical signs: skin disease, a heart murmur associated with coughing and/or exercise intolerance, a seizure disorder, 'fly-catching' behaviour, otitis media with effusion or any other debilitating condition which could be associated with pain or discomfort, such as pancreatitis, arthritis or intervertebral disc disease. Questionnaires were excluded if data were incomplete or obviously incorrectly entered.

### Statistical analysis

Comparisons of data between populations were performed using the Mann–Whitney *U* test for unpaired data. Spearman's rank correlations were used to assess the significance level of correlations between NeP score, weighted behaviour scores and QoL. The false discovery rate (FDR) of Benjamini et al. (2001) was applied to control for the increased risk of falsely significant results in multiple comparisons. All tests were two-sided and $P < 0.05$ was considered to be significant. Data are presented as median (range minimum–maximum, interquartile range, IQR).

## Results

### Data collection

Five-hundred and sixty-four questionnaires were answered. Incomplete or incorrectly entered questionnaires were excluded ($n = 303$). Two-hundred and one questionnaires were excluded because the diagnosis of CM/SM was based on clinical signs and was not confirmed by MRI; an additional 91 entries were also excluded because the section asking about MRI was left blank. Eleven entries were excluded because no breed was entered. Dogs were also excluded if they had a history of skin disease ($n = 21$), heart murmur associated with coughing and/or exercise intolerance ($n = 31$), epilepsy ($n = 6$), 'fly-catching' behaviour ($n = 28$), otitis media with effusion ($n = 33$) or any other debilitating condition apart from CM/SM ($n = 20$). Following these exclusion criteria, 122 questionnaires were included in the analysis.

### Animals

Of 122 CKCS included in the study, 95 (78%) were from the UK, 11 (9%) from the USA, six (5%) from the Netherlands, four (3%) from Canada, four (3%) from Australia, one from Bermuda and one from the Czech Republic. The median age was 54 months (range 12–132, IQR 40.5–80.0 months) and the median weight was 8.5 kg (range 5.0–13.7, IQR 7.7–10.0 kg). Fifty dogs were male (29 neutered) and 72 were female (42 neutered). Eighty-four (69%) dogs were being treated with either one or a combination of the following drugs: gabapentin, furosemide, pregabalin, prednisolone, carprofen, cimetidine or omeprazole.

### Behavioural changes and quality of life

A significant positive association was found between NeP score and ratings for stranger-directed fear, non-social fear, separation-related behaviour, attachment behaviour, excitability and pain sensation (Table 1). The NeP score had a significant positive association with QoL score (Fig. 1). NeP was negatively associated with exercise level ($r_S = -0.5$; $P < 0.0001$; FDR 0.0045) and ability to settle for rest ($r_S = -0.26$; $P = 0.0018$; FDR 0.0068). However, only 9/120 (8%) of owners described their dog as having a fairly poor

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