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# To be blamed or pitied? The effect of illness on social behavior, cytokine levels and feed intake in undocked boars



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#### ABSTRACT

Tail biting is detrimental to animal welfare and has negative consequences for producer economy. Poor health is one of the risk factors for tail biting. The first aim of this study was therefore to test for links between health status and behavior related to tail biting at the individual level. The second aim of this study was to test whether variation in cytokines was related to variation in social behavior. These small molecules produced upon immune activation are known to influence behavior both in the direction of withdrawal and increased aggression. This could potentially increase non-functional social behavior and thereby the risk of a tail biting outbreak. To investigate this, we collected behavioral data, health data, feeding data and blood samples from undocked boars at a test station farm in Norway. We compared groups with three different diagnoses: osteochondrosis diagnosed by computer tomography scanning (OCSAN), osteochondrosis diagnosed by clinical examination (OCCLIN) and respiratory tract disease (RESP), with healthy controls (CTR). We tested whether the diagnoses were associated with feeding and growth, social behavior and cytokine levels. We then tested whether there were correlations between cytokine levels and social behavior. We also provide raw data on cytokine levels in the extended sample (N = 305) as there are few publications on cytokine levels measured in pigs living under commercial conditions. OCCLIN pigs visited the feeder less, and fed longer compared to CTR pigs. Pigs diagnosed with RESP showed a large drop in growth the first week after filming, which corresponds to the week they were likely to have been diagnosed with illness, and a tendency to compensatory increase in the week after that. Social behavior differed between experimental groups with OCSCAN pigs receiving more social behavior (both aggressive and nonaggressive) compared to CTR, and RESP pigs tending to perform more ear- and tail-biting than controls. There were no differences in absolute levels of cytokines between categories. However IL1-ra and IL-12 showed correlations with several behaviors that have been shown by others to be associated with current or future tail biting activity. To our knowledge, this is the first published study indicating a role for illness in non-functional social behavior in pigs and the first showing a correlation between cytokine levels and social behavior.

#### 1. Introduction

Tail biting is one of the gravest problems in intensive pig production [1–3] and indicates that the environment is not meeting the needs of the pigs. Several risk factors for tail biting are known, but many of them are only described at group-level. How they influence the behavior of the individual animals and by which mechanisms they work are poorly understood. Based on epidemiological studies, case control studies and clinical reports, poor health is considered a risk factor for tail biting.

Farms with health problems are considered to have a higher risk of a tail biting outbreak [4]. The risk of tail biting damage on farms with rectal prolapse and respiratory disease was increased [5]. Deworming was found to reduce tail biting [6] and pigs vaccinated against Lawsonia intracellularis had lower percentage of culling due to social stress and cannibalism than unvaccinated controls [7]. Both leg disorders and respiratory inflammation have been found to be highly correlated with tail damage [8,9]. While these references show that the relationship between health and behavior warrants investigation, they cannot be

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used to ascertain the direction of effect (i.e. what came first: inflammation or tail biting) and it is also not clear whether the relationship between health and behavior is direct or through a third mechanism such as improved nutritional status [5].

A possible mechanism by which health could influence behavior is through the effect of cytokines on neurotransmitter systems. The knowledge of cytokine effects on behavior comes from descriptions of the behavioral consequences of naturally occurring illness, so called 'sickness behavior' in humans [10] and from the side effects experienced by human patients subject to immune therapy for example for hepatitis or metastatic cancer [11,12]. Sickness behavior is mainly elicited by the pro-inflammatory cytokines interleukin 1 beta (IL-1\beta). tumor necrosis factor alfa (TNF-α) and interleukin 6 (IL-6) and manifests as anorexia, lethargy and decreased social motivation [10]. It is possible that the change in social motivation has a negative effect on the social dynamics in a group of pigs, increasing the likelihood of the ill pig becoming a victim. As a sick animal is weakened, others may actually prefer to compete with this animal for resources, as success is more certain than if engaging in a contest with a healthy conspecific. This mechanism has been described for male finches [13]. Severely ill animals would also have more difficulty escaping bullying from penmates.

However, lethargy and withdrawal are not the only behavioral changes brought about by cytokine increase. Depression, irritability and short temper, extreme emotional lability, tearfulness and cognitive impairment have been reported in human clinical studies on the effects of treatment with pro-inflammatory cytokines such as IL-2 and interferon alpha (IFN $\alpha$ ) [11,12,14,15]. There is also increasing evidence for a role of inflammatory proteins in aggression, and psychiatric patients with a diagnosis of intermittent explosive disorder had higher levels of IL-6 and C-reactive protein (CRP) than controls [16–18]. Through the effect of cytokines on behavior, pigs with a degree of inflammation that would not be severe enough to render them lethargic could potentially show aggression towards their penmates.

In order to test whether illness has a negative effect on social behavior we compared pigs diagnosed with respiratory tract disease or osteochondrosis (OC) with healthy controls. We predicted that illness would lead to a change in social behavior with more agonistic interactions, but as outlined above, we did not predict the direction of effect, having reasons to believe that pigs could both engage in and receive more agonistic behaviors. In order to look into whether cytokines can be mediators of the suggested effect of health on social behavior we tested whether any cytokines correlated with social behavior. We analyzed feeding behavior and feed intake to get additional information about how the diagnoses influenced the animals.

#### 2. Materials and methods

#### 2.1. Animals, housing and husbandry

The experiment complied with Norwegian legislation which states that experiments in which the procedures are similar to or less in severity than the insertion of a needle, does not need to be applied for. In the current experiment, the most severe procedure was blood sampling from the ear vein while the pigs were anaesthetized as part of routine procedures on the test farm. The boars in this study were part of the Norsvin genetic programme, and were sampled in the period from October 2014 to February 2015. The Norsvin boar test station is described in [19]. The pigs were purebred Landrace boars born and raised to 25 kg in 37 nucleus herds before they were transported to the test station. They were then between 65 and 84 days old. The boars were kept at the test station for approximately 2.5-3 months (the 'test period'). At the end of the test period they were either transported to the breeding facility or slaughtered, depending on the outcome of the test. This experiment was carried out towards the end of the test period when the boars reached a weight of 120 kg (137-190 days old) upon

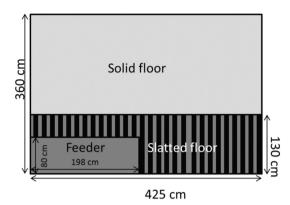


Fig. 1. Pen layout within which the experimental boars were housed, prior to, and during the extent of the study.

which they were subjected to scanning by computer tomography (C-T). The boars were housed in pens in groups of 12 (Fig. 1). A pen contained pigs from different farms. The pigs were assigned to a group upon arrival to the test-station and the groups remained unchanged throughout the testing period. The pigs were vaccinated against *Actinobacillus pleuropneumoniae* on arrival at the farm and again 3 weeks later. Pigs were fed ad-libitum by means of the FIRE transponder station which contains a scale so that the pig is weighed every time it enters the feeder (FIRE; Osborne Industries Inv., Osborne, KS, USA). Light was turned on from 05:10 am to 09:10 pm and controlled by an automatic timer. Pens were cleaned daily and fresh sawdust sprinkled on the solid lying-area. Each pen received a handful of hay every day.

#### 2.2. Health monitoring

Health was monitored in two ways as part of the normal husbandry procedures: firstly, the caretakers observed the animals for lameness, coughing, diarrhea and other visible signs of illness when they entered the pen to clean it every morning. Secondly, a software system was set up to provide a daily list of animals whose feed-intake had dropped below 50% of the pen mean. These animals were then examined, and their body temperature was measured using a rectal thermometer. Animals that showed an increase in temperature or other signs of illness were treated according to a standard protocol. An electronic health record was kept for each individual. Animals with a diagnosis of respiratory tract disease or osteochondrosis diagnosed clinically (i.e. a high osteochondrosis score from the computer tomography (CT) scan did not result in any treatment) were treated in the following way: Respiratory tract disease was treated with benzylpenicillinprocain at 20.000–60.000 I.U. kg<sup>-1</sup> (Penovet vet., Boehringer Ingelheim, Denmark) for three days and meloxicam at 0.4 mg kg<sup>-1</sup> (Metacam vet., Boehringer Ingelheim Vetmedica) for one day. Osteochondrosis was treated with a single injection with dexamethasone at 0.06 mg kg<sup>-1</sup> (Dexadreson vet., MSD Animal Health) and a mixture of selenium and vitamin E (Selevitan vet., Boehringer Ingelheim). If lameness co-occurred with the stiffness characteristic of osteochondrosis, they also received benzylpenicillinprocain for two to three days.

### 2.3. Computer tomography (CT)

When the pigs reached 120 kg, they were all CT-scanned, among other things to diagnose osteochondrosis (OC) in the elbow and knee joints [19]. On the morning of scanning, they were allowed to walk from their home-pen into the waiting room by the CT-scanner. There they were housed in one of 24 individual pens with access to water but not food. They were sedated by an intramuscular injection of 8 mg kg $^{-1}$  of azaperon (Stresnil: 40 mg ml $^{-1}$ , Janssen). When sedated, they were moved to the scanner by means of a carriage, scanned and returned to the pen. They were kept in the individual pen until the next

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