Do dairy cows with mastitis show signs of sickness behavior? - and why should we care?
Presentation

• Ethologist, study animal behaviour

• PhD: Pain sensitivity and responses toward acute stress in dairy cows (1999-2004)

• Special interests: pain, injury & misery

Recent bovine projects
• Pain associated with liver biopsy sampling

• Behavioural changes and pain during...

Today: basic biology – and the science behind - not recommendations regarding drugs or other therapy
Outline

Disease behaviour

- what is it?
- why are animals changing behaviour?
- what happens in the body?
- where is this known from?
- what about mastitis?
- why should we care?
Interesting topic….

Google: > 15 mio hits

![Publication year vs. Number of papers](chart.png)
Disease behaviour

- **Earlier**: behaviour during disease = no function
- Unpleasant, but banal part of being sick
- Has not received same focus as other types of behaviour
- Interest started in the 80ies

Common term for behavioural changes during disease

- Sleeps
- Tremble
- No appetite
- Avoid company
- Hygiene
Seek company

Motivated to exercise

Likes to eat at lot

Seek isolation

Immobile

Do not experience hunger

Disease changes motivation and needs
In nature

- Selection pressure from disease = large consequences for the evolution of behaviour

- $\Delta$ behaviour and fever = consistent response across animal groups and pathogens $\Rightarrow$ evolutionary biological advantage

- Sleeps, no appetite, trembling, isolation, hiding, immobile $\Rightarrow$ evolutionary survival value ($\downarrow$ spread of disease, risk of predation)

- Fighting pathogen, energy to increased metabolism, heat

Well organised biological strategy (behaviour, physiology, metabolism), facilitates the fight against pathogens and can be crucial for survival in nature
How is this known?

- Experiments with mice/rats as part of studies of disease biology and the immune system
  - Behaviour before/after disease
  - Spontaneous/induced (LPS)

- LPS: lipopolysaccharide = parts of cell walls of pathogens → symptoms and fever

- Activity in the immune system (hormone-like substances = cytokines)
What happens in the body?

Invading organisms cascade af immun. responses = acute phase response
Secretion of inflamm. mediators
CYTOKINES

Disease behaviour
Fever
Pain sensitivity

Disease behaviour facilitates survival ⇒
behaviour is a component of the immune system

Initiating metabolic and behavioural changes

Brain

Periphery
What do sick rodents do?

Typical behavioural changes during disease

↓ activity, exploration, (apathy)
↓ grooming/comfort ⇒ dirty fur
↓ feed intake
↓ water intake
↓ social behaviour
↓ memory and learning capacity

↑ pain sensitivity
↑ sleep
↑ confusion
↑ trembling
↑ depressed mood (anhedonia)

Both spontaneous and in tests, not specific for animal species or pathogen
How do they feel?

Methods from psychology
Aversion
• Conditioned taste/aversion paradigm

• Rats receive LPS in water tasting like sugar (which they like very much)
Later they will avoid sugar-taste

Animal priorities and needs
• Operant conditioning – work for access to resources

• Disease ⇒ social animals seek isolation ⇒ Δ motivational priorities

• Sensitive towards the environment: ↓ nestbuilding at 24°, but not at 6°, where the survival of the pups are threatened

Disease facilitates survival by re-organising needs ~ a motivational system, competing with others
What about cattle?

What happens when they get sick?
Seek company
Likes to exercise
Eats a lot

Seeks isolation
Immobile
No hunger

Disease changes motivation and needs

Design of sickness pens
Mastitis
Is mastitis painful?

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<tbody>
<tr>
<td></td>
<td>Veterinarians</td>
<td>Vet. students</td>
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</tr>
<tr>
<td>Toxic mastitis</td>
<td>7 (1-10)</td>
<td>7 (3-10)</td>
<td>9 (1-10)</td>
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<tr>
<td>Clinical (clots)</td>
<td>3 (1-10)</td>
<td>5 (1-10)</td>
<td>2 (1-10)</td>
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Yes, but even veterinarians disagree as to how painful
Research in mastitis?

Publications:
• Web of Science (Oct. 2012):
  - 5399 papers on ”mastitis and cow”
  - a handful about behaviour during mastitis (<5 years old)
  - only 23 included pain as a topic
  - none has integrated the two concepts

Analogy: humans
• Pain & illness during human mastitis, especially during nursing = taken for granted
Behavour during mastitis?

- Dairy cows in tie stalls
- Mastitis induced by injection of live *E. coli* or LPS in the udder
- High degree of control
- Normal behaviour + pain indicators
- Compare days ~ clinical signs of disease

Fogsgaard et al., 2012; Siivonen et al., 2011
Fogsgaard et al. (2012):

- 20 dairy cows (1. lactation, 3-6 w after calving)

- Tie stalls, empty neighbouring stalls

- TMR, maize silage

- Milked in the home stall twice/d

- Controlled health status (SCC < 27,000 cells/mL)
Systemic symptoms of mastitis
Eating and ruminating behaviour

Eating and ruminating reduced during the first 24h, where the clinical symptoms were clearest.
Comfort behaviour and standing idle

Reduced comfort behaviour and standing idle in the initial 24h
Yes, dairy cows do show typical behavioural changes during disease.

Mastitis → sickness behaviour

But was there something that did not fit?

Fogsgaard et al., 2012; Siivonen et al., 2011
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Dairy cows with induced mastitis show signs of disease and pain.
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- Location of inflammation on body probably influences the behaviour
- Knocking out sensory input from infected quarters would help us answer

**Dairy cows with induced mastitis show signs of disease and pain**
Behaviour during mastitis?

- Classic examples of sickness behaviour
  - ↓ eating, feed intake
  - ↓ ruminating
  - ↓ comfort behaviour

- Behavioural Δ corr with local and systemic clinical signs
  - SCC, milk yield and rectal temperature

- Very low dosis ⇒ adfærd og klinik normaliseret indenfor 48 h

- ↑ standing idle probably related to pain/soreness of the infected quarter
  - location of infection and flooring might affect the expression of sickness behaviour

Yes, cattle do show sickness behaviour
Why should we care?

<table>
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<th>Basic knowledge</th>
<th>Allow sickness behaviour</th>
<th>Optimize management</th>
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<tr>
<td>• Immunesystem</td>
<td>• Promote healing?</td>
<td>• Identify sick individuals</td>
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<tr>
<td>• Motivation</td>
<td>• Meet needs ⇒ less discomfort and frustration, better welfare</td>
<td>• Improve diagnostics</td>
</tr>
<tr>
<td>• Disease models</td>
<td></td>
<td>• Housing of the sick animals?</td>
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<td></td>
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<td>• Recovery – back to duty?</td>
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<td>• (Danish study just started)</td>
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A big potential and lots of work to do 😊
Challenge

In order to get exploit the potentials within sickness and pain in dairy cow production we need to be able to separate the concepts – at least scientifically
Effects of sickness and disease

- Might mix up results ~ pain / disease
  - the lack of lying in the studies just presented
  - Recent results about changes in pain sensitivity?
Pain sensitivity during mastitis

• Earlier slide: inflammatory mediators $\rightarrow$ increased pain sensitivity

• Older studies: hyperalgesia during and after spontaneous mastitis (Fitzpatrick et al., 1998)

• Mild to moderate spontaneous mastitis

• What happened during acute clinical E. coli mastitis?
Hyperalgesia and allodynia

- **Hyperalgesia**
- **Allodynia**

Relationship between stimulus intensity and pain sensation in normal and injured conditions. Mizumura, Nagoya J. Med. Sci. 60, 1997
Thermal nociceptive stimulation

• Radiant heat ⇒ specific for heat sensitive receptors

• No/very limited handling of the animals

• Can be applied all over the body
Description of laser

- Computer controlled, invisible CO$_2$-laser
- Wave length: 10.6 $\mu$m
- Diameter: 0.6 cm
- Laser pointer attached to aim
- Stimulation stops at preset time or by keypress
- Placed on trolley
Validation of laser test

Latency to move leg, sec.

Laser power output, Watts

Kicking, %

Valid measure of nociception with large variation

- chosen power

Herskin et al., 2003
Pain sensitivity during mastitis

• A subsample of our cows were tested for thermal pain sensitivity using laser stimulation

• Showed reduced responses toward stimulation directed at hind legs and udder during days with clinically signs

• Pos correlations between rectal temperature and latency to respond

• Here, the disease might have blunted the responses to pain

Complex interactions exist between pain and disease behaviour
Effects of sickness and pain

• Need to integrate studies of disease and pain and be able to separate them

• Sick animals + nerve block / pain relief

• Healthy animals + model of udder pain without disease

Important for understanding of the concepts and for improvements of practice in the future
Take-home messages

• Behavioural changes during disease are due to a complex interaction between immunesystem and brain

• Disease behaviour has a function = promote survival

• Disease ~ motivation ⇒ animal needs and priorities change
Curious?


Thank you for the attention