SUMMARY

Animals co-exist with many other small organisms, some form a symbiosis, others are harmful to the organism and induce various types of diseases, which are often accompanied by symptoms and behavioural changes. On one hand, pathogens can induce such behavioural alterations for their benefits. On the other hand, an acute infection can lead to behavioural changes that are beneficial to overcome the animal's threat. These behavioural adaptations are summarised under the term sickness behaviour (Hart, 1988; Hart and Hart, 2019). Many studies have shown how the immune system works to overcome the infection and alter the animal's innate behaviour (Dantzer and Kelley, 2007). However, the neuronal correlates underlying sickness behaviour are poorly understood.

The present work provides new insights in two behaviours that are significantly altered in response to a sepsis-like bacterial infection. A model for sepsis-like bacterial infection was necessary to investigate potential changes in behaviour of *Drosophila*. Further, it was necessary to ensure the best possible way to reliably induce an infection that allows for comparative analysis of behaviour and the underlying neuronal activity. The bacterium *Erwinia carotovora carotovora* (*Ecc*) turned out to be a suitable model organism to infect the fly. The bacterium induces a mild course of infection which makes comparative behavioural analysis possible. Amongst the behaviours altered following bacterial infection, I was able to demonstrate that an infection with *Ecc* reduces feeding behaviour and increases the fly's spontaneous horizontal locomotor behaviour.

Further, I could demonstrate that the behavioural changes are accompanied by distinct patterns of increased neuronal activity in the ventral nerve cord (VNC) of the fly. In contrast, the activity in the brain appeared rather diffuse and inconspicuous. Since the fly's VNC has been less well studied compared to the brain, I characterised the expression patterns of different peptidergic and aminergic neurons in the VNC. The orchestration and coordination of many behaviours of the fly involve the recruitment of neurons located in the VNC of the fly. However, the investigation of neuronal circuits have so far been focused on the wiring and connectome of neurons which are located in the brain. The description of these neurons helps to complete the picture of neuron circuits and neurotransmitter distribution in the CNS of *Drosophila*.

I compared the expression pattern of the peptidergic and aminergic neurons in the VNC with the increased neuronal activity pattern after sepsis-like bacterial infection. The comparison revealed a similarity between the expression pattern of Leucokinin (Lk)-expressing neurons (LkNs) and Lk receptor (LkR)-expressing neurons and the increased neuronal activity pattern after sepsis-like bacterial infection. Lk- and LkR-expressing neurons were previously demonstrated to alter feeding and locomotion behaviour. Therefore, I have analysed the role of abdominal leucokinin-expressing neurons (ABLk) in the control of the behavioural alteration following a sepsis-like bacterial infection. LkR Knock-Out experiments revealed a potential role of the Lk-signalling pathway in the reduction of feeding behaviour. However, Knock-Out of LkR did not induce any evident changes in spontaneous horizontal locomotor behaviour. Searching for another neurotransmitter that may potentially correlate with the demonstrated neuronal activity pattern to the behavioural changes, two LkNs per side of the VNC, situated anterior-laterally in the abdominal ganglion (AG) were immunoreactive for tyrosine hydroxylase (TH), the rate limiting enzyme for the dopamine biosynthesis. Downregulation of the biosynthesis of dopamine (DA) through RNAi, specifically in LkNs resulted in no alteration of feeding behaviour but a significant decrease of spontaneous locomotor behaviour after bacterial infection.

It is worth noting, that the here described infection-triggered behavioural alterations represent examples of sickness behaviour which do not directly improve the fitness and survival of the animal. Rather, the behaviour appears to be induced as a quick stereotyped response to the ongoing infection states. It may consequently serve for reducing a possible further infection by escaping and reducing the risk of a potential pathogenic hazard for the offspring. My data indicate that a group of anterior-lateral ABLks in the AG which co-express DA convey the behavioural adaptation in response to a bacterial infection with *Ecc*. However, the presented data of this work allow for the assumption that these two neurotransmitters cooperatively orchestrate the demonstrated infection-induced behavioural changes.