and H4 and either down- or up-regulation of several hundreds of genes, as was evident from the DNA microarray-based global transcriptional analysis. The general trend was up-regulation of genes involved in detoxification and chaperone activity, including several genes that have previously been found to be involved in life span determination in *D. melanogaster*, and down-regulation of genes involved in different metabolic pathways. These findings support the hypothesis that life span extension may be caused by overall generalized changes in epigenetic regulation.[48]

21.3.2 Sodium Butyrate

In several studies (Table 21.2), life-extending capacity was also shown for sodium butyrate (SB), a short chain fatty acid having HDAC inhibition activity and known to markedly influence the processes of cell growth, differentiation and apoptosis in both normal and transformed cells.[49,50] In *D. melanogaster*, an increase of both mean and maximum life span by 25.8% and 11.5%, respectively, was observed due to one-off treatment with SB.[51] Later, an increase in mean and/or maximum life span and a decrease in mortality rate after SB treatment were observed by other authors.[52–55] SB at concentrations varying from 10 to 40 mM demonstrated the potential to increase life span, whereas SB treatment at higher doses (more than 100 mM) decreased longevity.[51,52] In some cases[51,55] effects depended on whether the line used was short- or long-lived. The life-extending effects obtained were unlikely due to the decreased reproductive investment, because no reduction in reproductive activity (fecundity) was revealed in SB-treated female flies.[52] In some cases, life span improvement was accompanied by an increase in locomotor activity[55] (see also Figure 21.1), which is often considered as a marker of health and aging.[56]

Treatment with SB caused elevated acetylation levels at histone H3,[51,57–59] whereas the level of acetylation of histone H4 remained unchanged.[59] Histone H3 with elevated acetylation levels was found at the promoter of the *hsp22*,[57] *hsp70*,[58] and *hsp26*[59] genes. Also, SB affected the structure of chromatin at the site of cytogenetic location of the *hsp70* gene on the polythene chromosome.[60] Accordingly, elevated levels of expression of *hsp22*, *hsp26*, and *hsp70* genes were found in SB-treated flies.[51,57–60] According to Zhao and co-authors,[51,57] these findings suggest that the alterations in histone acetylation and, thereafter, the expression of chaperone genes, may contribute to the life-extending effects of SB and other HDACIs in *D. melanogaster*.

Other mechanisms, however, may also be contributing. In recent research by St Laurent and co-authors,[54] treatment with SB-supplemented food rescued the early mortality of flies with the pesticide rotenone-induced Parkinson's disease. In this model, SB was selected as a therapeutic candidate because it is known to be able to correct the disrupted HDAC activity in Parkinson's disease and other neurodegenerative disorders. The SB-mediated rescue of rotenone-induced Parkinson's disease was associated with elevated dopamine levels in the fly brain. At the same time, treatment