

Summary

In the last couple of decades, there has been more attention for the relation between health status and psychological processes. The results of studies on the effectiveness of psychological interventions in optimizing health outcomes are promising. However, the underlying processes are not yet fully elucidated. Moreover, it is not often investigated whether adding innovative psychological intervention tools to psychological intervention can optimize the effectiveness of interventions. The aim of the current thesis was to examine the effectiveness of innovative psychological interventions on health optimization by (1) evaluating the effectiveness of innovative psychological tools, i.e., serious gaming (games that contain educative as well as entertaining components), verbal suggestions, and internet-based interventions, to optimize health behavior and psychophysiological outcomes; (2) providing a concise overview of the currently existing evidence of psychological interventions in optimizing immune function in response to *in vitro* or *in vivo* immunological as well as psychophysiological challenges; and (3) incorporating several self-reporting, behavioral and psychophysiological outcome measures with (psycho)physiological stressors to evaluate the effectiveness of psychological interventions on health outcomes.

In **Chapter 2**, we investigated the effectiveness of serious gaming on food-related outcomes and physical activity. We included healthy participants and randomized them to a serious gaming condition, in which subsequently serious games were played for half an hour or a control condition, in which control games were played. The serious games were based on (1) transferring knowledge, (2) priming (i.e., a subconscious process that leads to faster recognizing of and/or reacting on a stimulus that has been observed previously) and (3) evaluative conditioning (i.e., changing the valence of a stimulus by repeatedly providing this stimulus together with other positive or negative stimuli) of health outcomes. The control condition contained games that were not health-related. Afterwards, participants were subjected to self-reported outcome measures, including a food choice task with healthy and unhealthy food products. In this food choice task, participants first had to indicate their preference for each of the healthy and unhealthy food products, and subsequently had to choose between a healthy and unhealthy food product. In addition to this task, observations of actual health behaviors were completed, in that it was observed whether participants took the stairs or the elevator to move from the first to the fifth floor, as well as observations of an actual food choice (healthy or unhealthy) to which people were subjected at the end of the experiment. We found that serious gaming during one session of half an hour could optimize

self-reported food preference. However, serious gaming did not affect actual food choice or physical activity. Playing these serious games for half an hour therefore provided a first step towards health optimization, although future studies should further confirm these findings.

To optimize the effectiveness of serious gaming, we investigated whether verbal suggestions can serve as an effective add-on tool in **Chapter 3**, as verbal suggestions directed at manipulating positive outcome expectancies already showed promising results in the placebo literature. In this randomized controlled trial, we specifically focused on optimizing food outcomes. The serious games and verbal suggestions in this study were primarily based on approaching healthy food items and avoiding unhealthy food items. Healthy participants were randomized to a serious gaming condition, accompanied or not with verbal suggestions, a verbal suggestions only condition, or a gaming control condition. Afterwards, participants were subjected to a self-reported food outcome measure (with questions regarding food preference and food choice, see **Chapter 2**), an implicit association task (a test in which participants had to associate food-related words to the label ‘positive’ or ‘negative’, as well as the label ‘healthy’ or ‘unhealthy’ as fast as possible) and a bogus taste test (a test in which participants were instructed to rate food on specific characteristics, but actually their food consumption was measured). We found that serious gaming, accompanied or not with verbal suggestions, resulted in a healthier implicit food preference. However, no effects were found for actual food consumption. There was some cautious support for the add-on effectiveness of the verbal suggestions, although future research should further elaborate on this topic due to the small effect sizes. Future research should address whether verbal suggestions actually are a significant add-on tool for serious gaming, as the current findings are limited to precursors of health behaviors (e.g., food preference) instead of actual health behaviors.

To further investigate the effectiveness of verbal suggestions in the context of psychological intervention tools, we investigated whether verbal suggestions can strengthen the effects of a brief relaxation intervention in **Chapter 4**. Previous research suggested that verbal suggestions are not only able to optimize health outcomes, but also to facilitate an adaptive stress response. In our randomized controlled study, we allocated healthy participants to a relaxation condition, accompanied or not with verbal suggestions, a verbal suggestions only condition, or a control condition. Afterwards, participants were exposed to a social evaluative stressor and we subjected participants to self-reported outcomes of state anxiety and well-being, as well as psychophysiological outcomes of heart rate, skin conductance, salivary cortisol and alpha amylase. We found that a brief relaxation

intervention, accompanied or not with a verbal suggestion, resulted in lower self-reported state anxiety directly after the intervention, but not in response to a social evaluative stressor. Therefore, the brief relaxation intervention, accompanied or not with verbal suggestions, provided a first step towards reducing self-reported anxiety. Future studies should focus on incorporating several kinds of verbal suggestions as well as adjusting the content of the stressor onto the content of the intervention.

Next, we summarized the existing literature concerning the effectiveness of psychological interventions in optimizing immune function. A concise overview of the current existing literature by a systematic review and meta-analysis is provided in **Chapter 5**. In this systematic review and meta-analysis, we included studies that incorporated a chemical, physical or psychophysiological challenge into the study design to evaluate the effectiveness of a stress-reducing psychological intervention. Hereby, more insights in the actual response of the immune system on a natural challenge could be gathered. Overall, we found modest support for the effectiveness of psychological interventions on immune function with most conclusive results for studies that incorporated *in vivo* immune-related challenges. However, the selected studies in this meta-analytic review were rather heterogeneous with respect to the incorporated study populations, psychological interventions, incorporated challenges and immune outcomes. Therefore, future research should carefully consider the incorporated challenge as well as the immune outcome parameters according to the included study population. This will also provide important insights for clinical practice, as it can be investigated whether a psychological intervention can possibly, at least partially, substantiate or reduce medical treatments in patients with chronic somatic conditions.

Finally, we aimed to evaluate the effectiveness of a combination of innovative psychological intervention tools on health outcomes, by including multiple chemical, physical and psychophysiological challenges into the study design, to provide an as robust as possible provocation. In **Chapter 6**, the study design is described, and in **Chapter 7**, the results are described. Participants received a 6-week e-health intervention containing internet-based cognitive behavioral therapy combined with serious gaming. Afterwards, participants were subjected to a BCG-vaccination, as well as a test day including psychophysiological stressors (i.e., a social evaluative stressor, a cognitive stressor, and a physical stressor). We subjected participants to self-reported outcomes of state anxiety and well-being. Furthermore, we incorporated immune outcomes, as well as psychophysiological outcomes of heart rate, skin conductance, and salivary cortisol and alpha amylase at baseline, directly after the

intervention, at the start and end of the test day and 4 weeks later. Finally, we determined the IgG antibody responses following the BCG-vaccination at 4 weeks follow-up. Although we did not find evidence for optimized vitality after the intervention, we found that participants in the intervention condition reported lower physical sensations, and fewer sleep problems after the intervention, as compared to the control condition. We also found that self-reported well-being was higher in the intervention group after the psychophysiological challenges. Although no significant group differences were found for the psychophysiological and immunological outcomes, the data provided preliminary support for differential outcomes on heart rate variables as well as increased immunoglobulin G (IgG) antibody responses at 4 weeks follow-up. In addition, differential chemokine outcomes were observed at the end of the test day in the intervention compared to the control condition, when specifically focusing on time effects for both groups separately. The intervention therefore provided a first step towards developing preventive strategies in optimizing health outcomes. Future research should include patients with somatic conditions to investigate whether the intervention can optimize health outcomes in a population at risk for health problems.

Taken together in **Chapter 8**, the findings of the present dissertation underline the potential effectiveness of innovative psychological interventions in optimizing health outcomes. We found preliminary support for the effectiveness of serious gaming, verbal suggestions and internet-based CBT on optimizing various self-reported, observational, immunological, and psychophysiological health outcomes. Incorporating multiple psychophysiological methods and challenges to evaluate the effectiveness of innovative psychological interventions on health outcomes provided more insights in the mechanisms underlying the potential effectiveness of these interventions.