Computer-Based Exercise Program

Effects of a 12-week intervention on mood and fatigue in pediatric patients with cancer

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BACKGROUND: Increasing rates of survival present a new set of physical and psychological challenges for children dealing with side effects during cancer treatment. Physical activity has been shown to be an effective strategy to reduce several side effects.

OBJECTIVES: The purpose of this pilot study was to determine the benefits of a 12-week computer-based exercise intervention on perceived physical, motivational, and fatigue syndrome and psychological state.

METHODS: Nine inpatient and outpatient pediatric patients with cancer participated in a 12-week intervention consisting of supervised computer-based exercise sessions. Participants completed measures assessing mood and fatigue pre- and postintervention.

FINDINGS: The intervention was feasible and provided preliminary evidence for the benefits on mood and fatigue in pediatric patients with cancer. The results promote the effectiveness of physical activity in pediatric oncology and call for continuing research in pediatric patients with cancer where sedentary behavior and the associated side effects are a growing concern.

TREATMENT OF CHILDHOOD CANCER IS AGGRESSIVE and associated with several side and late effects, including sickness, cardiopulmonary compromises, musculoskeletal sequelae, fatigue, mood fluctuations, and motoric and cognitive dysfunction (Costa, 2010; McCulloch, Hemsley, & Kelly, 2014; Miller et al., 2016). As a result of long-term hospitalization, some of these side effects are a consequence of reduced activity behavior (Götte, Taraks, & Boos, 2014). Impaired physical fitness and its consequences, such as reduced cardiopulmonary function, decreased muscle strength, and fatigue, have been reported during childhood cancer treatment (Braam et al., 2016; Fuemmeler et al., 2013).

Therapeutic treatment and scientific interest increasingly focuses on quality of survival. Although regular physical activity is primarily recommended for its beneficial effects on cardiorespiratory health and fitness, a growing body of evidence supports the positive psychological effects of exercise (Wegner et al., 2014). Evidence shows that exercise improves mental health by reducing anxiety, depression, and negative mood and by improving self-esteem and cognitive function (Ahn & Fedewa, 2011). Although the number of reports of the effects of physical activity on mental health is steadily increasing, particularly in the general public (Reed & Ones, 2006) and gradually in adult patients with cancer (Yang, Tsai, Huang, & Lin, 2011), no literature focuses on the beneficial effects of exercise on mood in pediatric patients with cancer.

Cancer-related fatigue (CRF) is one of the most frequent and severe symptoms experienced by pediatric patients with cancer during treatment (Spathis et al., 2015) and can continue even after treatment has ended (Hamre et al., 2013). CRF is multidimensional, with the most distressing symptoms affecting quality of life. CRF is generally characterized by feelings of overwhelming exhaustion and lack of energy and enthusiasm (Berger et al., 2015). Research using physical activity has shown a reduction in fatigue in adults during and after cancer treatment (Cramp & Byron-Daniel, 2012). The results relating exercise and reduced fatigue syndrome in pediatric oncology are discussed controversially because several studies have shown a positive influence of exercise on fatigue (Keats & Culos-Reed, 2008; Rosenhagen et al., 2011; Yeh, Man Wai, Lin, & Chiang, 2011), and some have shown no influence (Hinds et al., 2007; Takken et al., 2009).

Computer-based exercise in the form of active video games has increasingly been used as an innovative approach to movement therapy (Staiano...
“The relationship between physical exercise, psychological health, and the motivation to be physically and socially active is essential for treatment success.”

& Flynn, 2014) and shows a high degree of acceptance and positive effects on mood in adult patients with cancer (Jahn, Lakowa, Landenberger, Vordermark, & Stoll, 2012). Key reasons for computer-based exercise being suitable for use in vulnerable populations like pediatric patients with cancer are the positive emotional experience, the high fun factor, and the low to medium physical stress (Biddiss & Irwin, 2010; Graf, Pratt, Hester, & Short, 2009). In addition, active video games can be a safe opportunity for hospitalized patients to obtain regular physical activity (Rosipal, Mingle, Smith, & Morris, 2013) and offer the possibility of a self-selected exercise intensity, which has been shown to be more effective in promoting positive affective response than a predetermined intensity of exercise (Ekkekakis, 2009; Parfitt, Rose, & Birgess, 2006).

Compared to the exercise therapy in adult patients with cancer, exercise therapy in pediatric oncology is still in its infancy. The optimal exercise intervention modality, intensity, timing, and duration of an exercise intervention in pediatric oncology are difficult to determine.

As a consequence of the lack of activity recommendations in pediatric oncology, the purpose of the Physical Activity in the Pediatric Oncology (PAPO) pilot study was to test feasibility and effects of a 12-week computer-based exercise intervention on mood and fatigue in pediatric oncology.

Methods
Study design was approved by the ethics board of the German Sport University Cologne and the University Hospital of Cologne. All patients and parents gave informed consent for participation in the study and received medical clearance from their treating oncologist. Exclusion criteria consisted of the absence of informed consent, age younger than 6 years or older than 18 years, difficulty performing exercise sessions because of general physical or cognitive impairments, and lack of language skills.

The PAPO pilot study was a prospective study that took place at a single hospital. The recruitment of potential patients at the inpatient and outpatient wards began following study presentation and the submission of information materials. The first contact to patients and their parents occurred in close cooperation with the pediatric oncology medical team. To ensure local proximity to the medical care and accompanying therapy, exercise interventions were carried out in a separate room in the pediatric oncology ward. The appointments for the exercise session were done at a convenient time for the patient and in person from Monday to Saturday. Each session was planned to be about 45 minutes (including breaks), and the patient and provider decided exercise duration and intensity by choosing different types and amount of games and game levels. The study team decided together with the healthcare team whether each exercise session fit into the patient’s therapy plan. Each intervention was supervised by a sports scientist (an exercise professional), and parents and siblings were often present in the exercise units. There were no exercise sessions during infusion of chemotherapy drugs.

Computer-Based Exercise Intervention
The 12-week intervention consisted of supervised computer-based exercise sessions and was executed using an active video game console (Microsoft® Xbox 360 Kinect). Before and during each session, participants could choose between a fitness and gymnastics game, a sports game, a dance game, and three other adventure games. The games offered different exercise categories and difficulty levels and included aspects of endurance, strength, coordination, and dexterity. The different games could be played alone or together, with or against each other. Movements were captured by a sensor, projected on the screen, and analyzed and evaluated by visual and/or auditory feedback (e.g., “well done,” “stretch your legs more”), in addition to the evaluation and feedback of the sports scientist. During the games, the players moved in virtual realities, such as on a tennis court, on a beach volleyball field, or in a fitness center. For individualization of exercise therapy, the intensity and duration of each intervention session were self-selected and chosen depending on the patient’s age, individual aerobic capacity, and daily condition, as well as whether the patient was inpatient or outpatient. Heart rate was monitored for objective assessment and control of the current load during the individual sessions.

Assessment Parameters
Case history of the participant was gathered at baseline from the participants and their parents and subdivided into four parts. The first part consisted of the contact data for the family and the personal information of the child. Details about cancer diagnosis and other diseases of the child were requested in the second part. In
the last two parts of case history, the exercise history during and before disease were assessed, including kind of exercise, duration, and regularity. In addition, a regular 24-hour day during and before disease was divided into sleeping time, sitting time, lying awake in bed time, and active time.

MOOD
Participants completed an age-related modified paper-and-pencil MoodMeter® questionnaire directly before and after the exercise intervention at weeks 4, 8, and 12. The original computer-based questionnaire had two scales that assessed physical well-being (perceived physical state) and perceived psychological strain (short form of the Eigenzustandsskala [EZ-K], which translates to “personal state scale”). The perceived physical state scale has 20 adjectives divided into subdomains of perceived physical activation, perceived physical fitness, perceived physical flexibility, and perceived physical health. This test assess short-term mood changes in athletes was validated in a sample of 645 healthy people and patients of varying age (range = 17–86 years) and varying sport experience (Cronbach alpha = 0.82, intraclass correlation coefficient = 0.92) (Kleinert, 2006). The EZ-K, the second scale, uses 16 adjectives to measure perceived psychological strain and perceived motivational state (Nitsch, 1976). Psychological strain consists of subdomains of sleepiness, mood, calmness, and recovery. Motivational state consists of subdomains of self-confidence, willingness to seek contact, social acceptance, and readiness to strain.

The questionnaire was given in the participant’s native language, and participants were instructed to rate each adjective for how much it described their current state on a six-point Likert-type scale from 0 (not at all) to 5 (totally). For children, the MoodMeter has been used in a modified paper-and-pencil version excluding the original time limit (four seconds per adjective) (Vogt, Schneider, Abeln, Anneken, & Strüder, 2012). The current authors identified that, in German, no mood measurement instrument has been validated in pediatric patients with cancer, potentially because little attention is given to mood in pediatric oncology.

The scale order was reversed for negative adjectives to compare to positive and negative adjectives and to analyze scores. Adjectives were pooled into subdomains and averaged into the three dimensions (perceived physical state, perceived psychological strain, and perceived motivational state). A mean of the three measurements at weeks 4, 8, and 12 was calculated for pre- and postintervention and included in statistical analysis.

FATIGUE
Fatigue was assessed by the German version of the PedsQL™ Multidimensional Fatigue Scale at baseline and at weeks 6 and 12. It consists of a self-report of children (aged 8–12 years) and teenagers (aged 13–18 years). The scale was originally designed and tested in the United States by Varni, Burwinkle, Katz, Meeske, and Dickinson (2002). It includes six items each for the three dimensions “general fatigue,” “sleep/rest fatigue,” and “cognitive fatigue.” All items used a five-point Likert-type scale from 0 (never) to 4 (almost always). Scores range from 0–100, where higher scores indicate fewer symptoms of fatigue. The reliability of the original PedsQL Multidimensional Fatigue Scale for subscales and total scale was Cronbach coefficient of 0.83–0.93. Although the German version of the PedsQL Multidimensional Fatigue Scale was developed and tested only in the Centre of Pediatric Oncology at the University Frankfurt (Jung, Höhne, Varni, Klingebiel, & Landenberger, 2009), the decision to use it was because of the lack of validated German alternatives in measurement of fatigue in children and adolescents with cancer. All items were first pooled into the three dimensions and averaged into overall fatigue.

Statistical Analysis
MoodMeter dimensions of perceived physical state, perceived psychological strain, and perceived motivational state were checked for significant changes using Wilcoxon test for paired samples with the intra-individual factor measurement.

Fatigue syndrome values were checked for normal distribution with Kolmogorov–Smirnov test with Lilliefors correction. Significant changes were calculated using one-way repeated measures analysis of variance and Bonferroni post hoc comparison test. Only complete data sets of all three measurements were integrated into the analysis, which led to the exclusion of two participants (N = 7) concerning fatigue.

Power analysis was applied using G*Power, version 3.1. Statistical analyses were performed using SPSS®, version 23.0. P values less than 0.05 were considered statistically significant.

Results
Sample Characteristics
Types of cancer present in this pilot study were leukemia (n = 3), lymphoma (n = 3), sarcoma (n = 2), and neuroblastoma (n = 1). The standard treatment for the pediatric patients was adjuvant chemotherapy at the inpatient and outpatient ward of the Department of Pediatric Oncology at the University Hospital of Cologne.

A total of 9 patients (n = 6 female, n = 3 male) diagnosed with cancer aged 8–14 years were included in the study. At baseline, mean age of the children was 11.33 years (SD = 2.24), mean height was 148.56 cm (SD = 16.99), mean current weight was 39.82 kg (SD = 12.04), and mean weight before disease was 46.56 kg (SD = 20.02). Mean body mass index was 17.74 kg/m² (SD = 2.53), and the weight-for-age percentile was 48.11% (SD = 32.87). Mean time from diagnosis to the beginning of study was 58.22 days (SD = 62.02). There were no significant differences between girls and boys regarding these parameters. No adverse events and no dropouts were observed during the study.

A self-report about the average classification of a regular 24-hour day showed changes in the everyday life of the children.
before and during disease. A significant decrease was seen in active time per day from 6.11 hours (SD = 2.8) before disease to 2.39 hours (SD = 1.87) after disease, and a significant increase was seen in inactive time (sleeping, sitting, lying awake in bed) from 17.89 hours (SD = 2.8) before disease to 21.61 hours (SD = 1.87) after disease (p = 0.004). The specific kind of exercise changed with disease onset. Although children played football, table tennis, basketball, dancing, gymnastics, or swimming before disease onset, the activity during cancer was limited to walking or light aerobics.

Exercise Sessions
During the 12-week intervention, participants performed a mean of 10.67 exercise sessions (SD = 2.12) with an average duration of 48.53 minutes (SD = 14.85), including 5–10-minute breaks per session depending on type of exercise, drinking breaks, and type of video game. Overall exercise duration during the 12-week intervention was 517.89 minutes (SD = 178.63), with an average heart rate of 138.55 beats per minute (SD = 9.74).

Mood
The MoodMeter assessment demonstrated significant increases pre- to postintervention in ratings of perceived physical state, perceived psychological strain, and perceived motivational state (see Table 1). Significant positive differences in the subdomains of physical fitness, physical flexibility, mood, willingness to seek contact, self-confidence, and readiness to strain were found. Pre- and postintervention, no significant differences were found in physical energy, physical health, calmness, recovery, sleepiness, and social acceptance.

Fatigue Syndrome
A one-way repeated measures analysis of variance in overall fatigue syndrome and sleep/rest fatigue showed a significant effect for factor measurement (see Table 2). A post hoc comparison revealed a significant change from baseline to week 12 in sleep/rest fatigue only. The comparison from baseline to week 6 was not significant. Although the repeated-measures analysis of variance for overall fatigue syndrome showed a significant effect for factor

| TABLE 1. CHANGES IN RATINGS OF MOOD SCORE PRE- AND POSTINTERVENTION USING WILCOXON TEST FOR PAIRED SAMPLES (N = 9) |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| VARIABLE        | PREINTERVENTION | POSTINTERVENTION | MINIMAL SUM OF RANKS | z SCORE | p   |
| Perceived physical state | 3.55 ± 1.04 | 4.05 ± 0.64 | 1 | 2.55 | 0.011 |
| Physical energy | 3.98 ± 1.11 | 4.16 ± 0.69 | 6 | 0.41 | 0.686 |
| Physical fitness | 3.27 ± 0.84 | 3.97 ± 0.68 | 0 | 2.68 | 0.007 |
| Physical flexibility | 3.25 ± 0.90 | 4.02 ± 0.54 | 1 | 2.55 | 0.011 |
| Physical health | 3.6 ± 1.39 | 3.94 ± 0.93 | 3 | 1.9 | 0.063 |
| Perceived psychological strain | 3.49 ± 0.95 | 3.91 ± 0.68 | 1 | 2.58 | 0.017 |
| Calmness | 3.02 ± 0.95 | 3.5 ± 1.02 | 7 | 1.54 | 0.123 |
| Mood | 3.84 ± 1.09 | 4.48 ± 0.63 | 0 | 2.21 | 0.027 |
| Recovery | 3.2 ± 1.53 | 3.65 ± 0.58 | 11 | 0.99 | 0.323 |
| Sleepiness | 3.91 ± 1.08 | 4.03 ± 0.87 | 5.5 | 1.05 | 0.293 |
| Perceived motivational state | 2.7 ± 0.85 | 3.23 ± 0.8 | 0 | 2.67 | 0.008 |
| Social acceptance | 2.86 ± 1.33 | 3.21 ± 1.08 | 11 | 1.6 | 0.109 |
| Willingness to seek contact | 3.26 ± 1.16 | 3.83 ± 0.9 | 0 | 2.38 | 0.017 |
| Self-confidence | 2.7 ± 0.68 | 3.12 ± 0.83 | 1 | 2.39 | 0.017 |
| Readiness to strain | 3.19 ± 1.23 | 4.17 ± 0.72 | 0 | 2.52 | 0.012 |

Note. Variables were rated using a six-point Likert-type scale from 0 (not at all) to 5 (totally). A mean of the measurements at weeks 4, 8, and 12 was calculated for the pre- and postintervention scores.
measurement, the post hoc test revealed no significant differences between the means.

Discussion
This is the first study to examine the effects of a computer-based exercise program on mood and fatigue in pediatric patients with cancer. The computer-based exercise program proved feasible in the inpatient and outpatient hospital, and no dropouts or adverse events were observed in this pilot study. Significant positive changes were found for all three dimensions of the MoodMeter (physical state, psychological strain, and motivational state). In addition, a significant effect was found for factor measurement in overall fatigue syndrome and the subscale of sleep/rest fatigue after the 12-week exercise intervention.

This study provides results showing a positive effect on mood for a computer-based exercise intervention in a population of inpatient and outpatient pediatric patients with cancer. In all three dimensions of the MoodMeter and in the subdomains of physical fitness, physical flexibility, mood, willingness to seek contact, self-confidence, and readiness to strain, significant positive differences were found from pre- to postintervention. These findings confirm previous studies reporting the positive effects of exercise on mood in the general public (Reed & Ones, 2006), in healthy children and adolescents (Eime, Young, Harvey, Charity, & Payne, 2013), and in adult patients with cancer (Yang et al., 2011), and extend these findings to the current participants. In addition, the results demonstrate that the computer-based exercise intervention had an effect on physical state, as well as psychological strain and motivational state. Particularly in pediatric patients with cancer, the relationship between physical exercise, psychological health, and the motivation to be physically and socially active is essential for treatment success. The mechanisms underlying the link between exercise and acute changes in mood are not clear, but it is likely that changes in the concentration of different neurotransmitters (Matta Mello Portugal et al., 2013) and alterations in central neural activity (Erickson, Gildengers, & Butters, 2013) play a role.

However, which exercise intensity generates the best effects on mood, particularly in pediatric patients with cancer, is unclear. In the current study, an individual 12-week computer-based exercise program with a self-selected intensity was used. The justification for this choice is that the self-determination in terms of intensity and type of computer game might result in a positive affective response. The heart rate of about 138 beats per minute in the current study reflects a moderate energy expenditure and is in line with other references about energy expenditure in active video gaming (O’Donovan & Hussey, 2012; Worley, Rogers, & Kraemer, 2011). The participants described that they felt the exercise intervention created a distraction from the daily hospital routine, which could have a positive influence on mood. In addition, research regarding the impact of exercise on mood and other psychological conditions, such as anxiety in pediatric oncology, is warranted.

Although evidence exists that exercise has a positive effect on fatigue syndrome in adult patients with cancer (Cramp & Byron-Daniel, 2012), results relating to exercise and reduced fatigue syndrome in pediatric oncology are continually debated (Hinds et al., 2007; Takken et al., 2009). The results relating to fatigue indicate that children reported significantly lower sleep/rest fatigue after a 12-week computer-based exercise intervention. In addition, a significant positive effect for factor measurement in overall fatigue syndrome and the subscale of sleep/rest fatigue in the exercise intervention was found. These findings are in line with previous studies showing a positive effect of exercise on fatigue in children and adolescents with cancer (Keats & Culos-Reed, 2008; Rosenhagen et al., 2011; Yeh et al., 2011).

One of the main causes of fatigue in patients with cancer may be impaired physical performance (Dimeo, 2001). This impairment could result in increased dependence, reduced self-esteem, limitations in social activities and family life, and pessimistic mood. Low

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>BASELINE</th>
<th>WEEK 6</th>
<th>WEEK 12</th>
<th>p ANOVA</th>
<th>PARTIAL $\eta^2$</th>
<th>POWER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall fatigue syndrome</td>
<td>63.37</td>
<td>19.15</td>
<td>70.44</td>
<td>24.01</td>
<td>78.37</td>
<td>20.74</td>
</tr>
<tr>
<td>General fatigue</td>
<td>63.69</td>
<td>20.09</td>
<td>75</td>
<td>22.31</td>
<td>77.97</td>
<td>26.88</td>
</tr>
<tr>
<td>Sleep/rest fatigue</td>
<td>55.36</td>
<td>24.02</td>
<td>66.07</td>
<td>32.49</td>
<td>76.79</td>
<td>23.67</td>
</tr>
<tr>
<td>Cognitive fatigue</td>
<td>71.07</td>
<td>19.91</td>
<td>70.24</td>
<td>21.71</td>
<td>80.36</td>
<td>15.16</td>
</tr>
</tbody>
</table>

ANOVA—analysis of variance
Note. Total possible range of scores was 0–100. Only complete data sets of all three measurements were integrated into the analysis, which led to the exclusion of two participants concerning fatigue.
physical performance can be interpreted by the patient as a sign of poor health and may then increase psychological distress. In the current study, the participants indicated a significant decrease in active time and a significant increase in inactive time, such as sleeping, sitting, and lying awake in bed, as a result of the onset of disease. This change in the daily routine, including reduced activity levels, could result in higher rates of fatigue, but an implementation of regular exercise adapted to a patient’s day could fulfill the natural urge to move and generate positive effects on fatigue. The aspect of the self-selected intensity may also play a role in the positive interaction on fatigue. In addition to exercise intensity, positive effects on fatigue could be triggered by exercise duration. Although the current 12-week intervention could potentially show a long-term effect on fatigue, Hinds et al. (2007) found no effect on fatigue when examining an enhanced physical activity intervention across two to four days in hospitalized children and adolescents receiving treatment for cancer. Improving physical activity with a computer-based exercise program may reduce fatigue and psychological stress and increase quality of life.

Limitations

The interpretation of the results may be limited by the small sample size and lack of control group. Excluding patients from potentially beneficial interventions is always an ethical issue, and the authors wanted to give every child the opportunity to participate in the exercise program. The inquiry of mood before and after an intervention has the advantage that the result is directly related to the intervention. Studies providing longer-term follow-up are needed to determine if the intervention effects are short-lived or if any late-appearing or lasting benefits to the exercise exist.

Implications for Nursing

A computer-based exercise program is feasible in pediatric oncology clinical practice. To improve physical activity in an oncology ward, a mobile active video-game console would be an advantage. Having a variety of games (fitness or gymnastics, sports, dance, adventure) can potentially maintain or increase patient interest. A computer-based exercise intervention can be individually modified, can be guided without a qualified sports scientist, and is a safe opportunity for hospitalized patients. It is useful to educate the children and their families from the onset of disease about the possibilities and positive impact of exercise on the side effects of cancer treatment like mood fluctuations and fatigue. For the maintenance of exercise, the involvement and motivation of the families are also relevant. In the current study, parents and siblings were often present and participated in the exercise sessions. Evidence has shown that family involvement is associated with increased physical activity in the population of pediatric patients with cancer (Yelton & Forbis, 2016). Because of the complications caused by cancer and its treatment and changing health and motivational status of the children, it is important to arrange the exercise sessions on a flexible basis. This may offer an opportunity to increase the activity time during hospitalization.

Conclusion

This is the first study to demonstrate significant changes in mood and sleep/rest fatigue after a 12-week computer-based exercise intervention. The results of this pilot study underline the importance of implementing an exercise program in inpatient and outpatient pediatric oncology treatment. The exercise intervention evaluated is easily transferable to other clinic or community-based oncology practices to enhance patients’ physical activity, improve mood and fatigue, and manage treatment-related symptoms.

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