Physical Activity in Clinical Psychiatry

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Summary

1.1

Introduction

The general aims of this thesis were twofold: in the daily practice of clinical psychiatry, to investigate an exercise intervention in patients with major depressive disorder (MDD) and to measure physical activity and sedentary behavior in patients with severe mental illness (SMI).

The present chapter summarizes the design, process evaluation, results and predictors of adherence of an add-on exercise randomized controlled trial (RCT) in MDD patients – the EFFORT-D study. In addition, the chapter describes a separate observational study into physical activity and sedentary behavior in SMI patients, mainly with schizophrenia.

1.2

Summary of Findings

We designed a high quality pragmatic RCT testing exercise in MDD patients, since previous RCTs had various methodological flaws. In addition, the study population had to reflect daily clinical practice (the "real world"), since few previous RCTs were representative for MDD patients in specialized mental health care. We were also interested in a relatively long follow-up period, since the earlier RCTs did not exceed a period of four months. For ethical reasons, but also from a pragmatic perspective reflecting the regular add-on practice of exercise in the treatment of MDD, we designed an add-on observer-blinded exercise RCT. The design of the EFFect of Running Therapy on Depression (EFFORT-D) was described in **Chapter 2**.

In EFFORT-D, the study population was recruited from emergency inpatient units in addition to day hospitals and outpatient programs for affective disorders in the hospital organization of the first author. Eligible patients could participate if their score on the 17-item Hamilton Rating Scale for Depression (HAM-D17) was ≥14, indicating MDD. We randomized half of the eligible patients to an add-on exercise intervention (Running Therapy or Nordic walking). Planned frequencies were a 1h session twice per week for 6 months, with increasing intensity. Measurements were planned at

inclusion (T0) and at 3 (T3), 6 (T6), and 12 months (T12). The primary outcome measure was the expected reduction in depressive symptoms as measured by the HAM-D17. A mean reduction in HAM-D17 of 8 points was expected in the intervention group and 6 points in the control group. To detect this difference with an α (two-tailed) of 5% and a power (1-β) of 80%, using two equal groups and a standard deviation of 5 points, 100 patients were needed in each group. We planned to measure cardio-respiratory fitness using a submaximal bicycle test. Biometric information would be collected and blood samples would be taken for the measurement of metabolic parameters. In addition, co-morbidity with pain, anxiety and personality traits were study objectives, as well as quality of life and cost-effectiveness.

Chapter 3 presented the results of the process evaluation of the EFFORT-D study, based on the method of Linnan and Steckler [1]. Participant inclusion, dropout and no-show were analyzed. A relatively high number (N=135) of the originally eligible participants (N= 183) had to be excluded. Total participation was 80% lower than foreseen due to low inclusion rates and fewer actual exercise interventions. Doubt about sufficient motivation was the main reason given for not participating in the study. Lack of motivation, probably due to disease characteristics, was apparently the reason for the high dropout rates: 40% at 3 months and 80% after 12 months. We concluded that depression severity was the primary factor determining dropout, followed by the duration of the intervention. In patients with MDD, emphasis on motivational issues is therefore essential right from the start of an exercise intervention, and a tailored and stepped-care approach is advised for future implementation.

In **Chapter 4** we described the results of the EFFORT-D study. The main hypothesis was that add-on exercise in the intervention group would reduce depressive symptoms compared to the control group. This was rejected. Depression scores of both groups improved independent of exercise. The small numbers of participants (46 participants, of which 24 in the intervention group), led to a lack of power and thus precluded firm conclusions. However, the effect size was so small (Cohen's d was 0.18 in the intention to treat analysis and 0.10 in the per protocol analysis), that it would be highly unlikely that a larger trial could find a clinically relevant effect on depression. In contrast, the effects of the

intervention on fitness ($Wmax \cdot kg^{-1}$ and $VO_2max \cdot kg^{-1}$) were large: increases of 15% and 18.5%, respectively were found in the intervention group within a period of three months, compared to 0% and 3% respectively in the control group. Also, the effect on cardiovascular risk factors such as BMI, waist circumference and visceral fat were large, with Cohen's d effect sizes >0.8 in favor of the intervention group. These findings confirmed earlier research in patients with MDD, but in contrast with other studies, the increase in fitness in EFFORT-D was independent of improvement in depressive symptoms. Unfortunately, we were unable to measure inflammatory state because of insufficient blood samples for measurement of C-reactive protein (CRP) beside fat spectrum. Another setback was that the intended statistical analysis of follow-up data at 6 and 12 months was not possible due to excessive loss to follow up, in combination with a lack of completed electronic questionnaires with data on quality of life, anxiety, pain and cost effectiveness. Despite these problems, the EFFORT-D study is one of the few such studies conducted in a "real-life" setting in specialized mental health care. Other strengths of the study were the use of a submaximal Åstrand bicycle test to measure fitness and the measurement of metabolic parameters as secondary outcomes.

We concluded that the EFFORT-D study underlines the importance and need of an add-on exercise intervention in MDD patients to reduce cardiovascular risk in the future, independent of the desired effect on reducing depression. To motivate patients to exercise and to prevent disappointment – for which depressive patients are already susceptible – psycho-education should be offered that emphasizes the clear benefits of exercise on reduced cardiovascular risk and indicates that exercise will not also directly lead to a reduction in depression.

Intrigued by the high numbers of non-adherence not only to the intervention, but also to the study protocol, we speculated that we could use these results to confirm the predictors of non-adherence described by previous authors. We also postulated that personality factors of the participants might have associated with their adherence. **Chapter 5** documented our analysis of determinants of adherence. The definition of adherence was participation at 3 and/or 6 months in the overall study protocol (total N=42, adhered N=28) or intervention (total N=24, adhered N=9 in at least 10 exercise sessions). Potential determinants were age, BMI, tobacco and alcohol use, severity of depression

(HAM-D17), anxiety (BAI), fitness ($Wmax \cdot kg^{-1}$; $VO_2max \cdot kg^{-1}$) and personality traits (NEO-FFI) at baseline[1]. Unfortunately, numbers were too low for analyses on smoking, drinking and anxiety. 'Higher Agreeableness' on the NEO-FFI – defined as individuals who are orientated towards experiences, interests and goals of others – was associated with better adherence to the overall study protocol (OR=1.2, p=.03) and depression (HAM-D17) was negatively associated with adherence to the intervention group (OR=.70, p=.046). The latter finding supported our recommendation in the process evaluation (Chapter 3) that adherence to a MDD exercise program needs substantial support from professional caregivers. In future MDD studies, measurement of personality traits could possible identify potential dropouts at an early stage.

As mentioned in the introduction of this chapter, in a parallel observational study we measured physical activity and sedentary behavior in patients with SMI (mainly schizophrenia). We decided to investigate this topic based on recent literature emphasizing the health threat resulting from the lack of physical activity and sedentary behavior, especially in SMI patients. In addition, due to the scarcity of research into these behaviors in inpatients with SMI, little was known about their prevalence and magnitude. This led to the study described in **Chapter 6** involving 184 inpatients who wore an accelerometer for five days. The aim was to objectively measure the total activity counts per hour and percentages regarding sedentary behavior, light intensity physical activity and moderate to vigorous physical activity. Accelerometer data of SMI patients were compared with the data of 54 healthy ward staff. Patients showed significantly fewer activity counts per hour compared to the ward employees (p=0.02), although the differences were small (d=0.32). During the five-day period, patients were sedentary for 84% of the time, spent 10% in light intensity physical activity and 6% in moderate-to-vigorous physical activity. Age was the only significant predictor: higher ages predicted fewer total activity counts per hour. We concluded that decreasing sedentary behavior and improving physical activity in SMI patients should be a high priority in clinical practice.

[1]BMI: Body Mass Index; BAI: Beck Anxiety Inventory
$Wmax \cdot kg^{-1}$:Maximal external power output related to weight; $VO_2max \cdot kg^{-1}$: maximal oxygen uptake related to body weight; NEO-FFI: Neuroticism-Extraversion-Openness Five Factor Inventory.

Another analysis within these 184 patients was aimed at exploring the association between quality of life, as measured with the EuroQol-5D and WHOQol-Bref, and the objectively measured physical activity. Possibly modifiable psychological determinants that could influence physical activity in long-term hospitalized patients with SMI were also measured. The resulting study described in **Chapter 7** showed that physical activity was positively related with, and was predictor for, all quality-of-life outcomes except those in the environmental domain, independent of patient and disease characteristics. The biggest improvement in quality of life was seen during the change from sedentary to light activity. However, attitude and self-efficacy were not related to physical activity. We concluded that encouraging patients to shift from sedentary behavior to light physical activity could be enhanced by alternative, more integrated and peer-supported interventions.

1. Linnan L, A.Steckler (eds.): **Process evaluation for public health, Interventions and research**; 2002.