

Whole body vibration added to treatment as usual is effective in adolescents with depression: a partly randomized, three-armed clinical trial in inpatients

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Abstract There is growing evidence for the effectiveness of exercise in the treatment of adult major depression. With regard to adolescents, clinical trials are scarce. Due to the inherent symptoms of depression (lack of energy, low motivation to exercise), endurance training forms could be too demanding especially in the first weeks of treatment. We hypothesized that an easy-to-perform passive muscular training on a whole body vibration (WBV) device has equal anti-depressive effects compared to a cardiovascular training, both administered as add-ons to treatment as usual (TAU). Secondly, we presumed that both exercise interventions would be superior in their response, compared to TAU. In 2 years 64 medication-naïve depressed inpatients aged 13–18, were included. Both exercise groups fulfilled a supervised vigorous training for 6 weeks. Depressive symptoms were assessed by self-report (“Depressions Inventar für Kinder und Jugendliche”—DIKJ) before intervention and

after weeks 6, 14 and 26. Compared to TAU, both groups responded earlier and more strongly measured by DIKJ scores, showing a trend for the WBV group after week 6 ($p = 0.082$). The decrease became statistically significant for both intervention groups after week 26 ($p = 0.037$ for ergometer and $p = 0.042$ for WBV). Remission rates amounted to 39.7% after week 6 and 66% after week 26, compared to 25% after week 26 in TAU. These results provide qualified support for the effectiveness of exercise as add-on treatment for medication-naïve depressed adolescents. The present results are limited by the not randomized control group.

Keywords Exercise · Physical activity · Whole body vibration · Sports · Depression · Adolescents

Introduction

Depression is a major psychiatric condition in childhood and adolescence worldwide [6]. The prevalence rates reported

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for Major Depression oscillate between 11.4% in the USA [68], 10.5% in a large European cohort [12] and up to 12% in the group of adolescents and young adults aged 14–24 in Germany [22, 36]. In line with the abovementioned, the number of patients under 18 requiring hospital treatment for depression has tripled within the years 2004–2012 [9]. The clinical guidelines for the treatment of adolescent depression in most countries report evidence for psychotherapy (cognitive behavioral therapy or interpersonal therapy), pharmacological interventions (mostly SSRI) or the combination of both, which was found to be the most effective (remission rates 37%) [51]. An elevated risk of suicide-related events under monotherapy with fluoxetine in combination with the other side effects of pharmacotherapy has engendered a decline of antidepressant demand and an increasing quest for alternative treatment approaches [35, 48]. One alternative treatment option in the focus of recent research is physical activity [16]. It is mostly side-effect free, and has secondary positive effects on somatic variables such as obesity [63]. A major issue in treatment approaches with physical activity is the difficulty to motivate patients to exercise due to the depression inherent listlessness [13, 38].

Physical exercise for treatment in adult depression

In 2013, the Cochrane collaboration reviewed 39 studies in total assessing the effectiveness of physical exercise as treatment for depression in adults. A moderate effect of physical exercise was found in comparison to no treatment or a control condition [16]. When compared to psychotherapy and pharmacological interventions, physical exercise was equally effective [16]. These results are in line with previous meta-analysis, but inconclusive referring to the specific type of physical exercise (intensity, frequency, duration, setting) to gain the highest anti-depressive effect [17]. The latest meta-analysis from Stanton and Reaburn found a supervised aerobic activity, with a frequency of three times a week at moderate intensity for a minimum of 9 weeks to be the most effective [71]. The causal agents for the positive effect of physical exercise on adult depression are elaborately studied but far from being established. It is assumed that a complex interaction of psychological and neurobiological mechanisms leads to the decline in depressive symptoms [59, 73]. Some psychological mechanisms pointed out are the strengthened feeling of self-efficacy, distraction, or the positive effects of social interaction and enjoyment [59]. Referring to the biological mechanisms on the transmitter level, the changes in monoamines, in the hypothalamic–pituitary–adrenal axis or in the production of β -endorphins are in the focus [59]. More recent research investigates the anti-inflammatory effect of muscular activity (e.g., decrease in IL-6, 8, 10, TNF- α) and the increase of BDNF or IGF-1 under exercise [18, 20, 28, 64, 80, 81]. It is hypothesized that

those mechanisms lead to a neurogenesis in the hippocampus crucial for the anti-depressive effect [28, 40–43, 49, 52, 75, 79]. Furthermore, BDNF-genotype (BDNF-Val-66-Met polymorphism) is suspected to influence the response to anti-depressive treatment by exercise [14, 25, 30, 37, 53].

Physical exercise for treatment in depressed adolescents

Studies on the effects of physical activity in the treatment of adolescent depression are far from being as numerous and well designed as in adult depression. Concerning the underlying mechanisms of action the state of science is even less. Studies either lack a sufficient number of participants or hold methodological weaknesses making findings inconsistent [33, 47, 66]. In adolescents, much of the research has been correlational or cross-sectional and in school-based, general-population or at-risk samples. In this line a recent multi-center cross-sectional study found physical activity being negatively associated with depression and anxiety symptoms in a school-based sample of 168 schools worldwide [54]. In a Cochrane Review from 2006, five of 11 studies demonstrated a significant difference in depression severity in favor of the exercise condition. More recent reviews found that physical activity had potentially beneficial effects for reducing depression, but did not comprise any clinical RCT [7, 10]. To conclude, only very few interventional studies tested the effect of physical exercise in the treatment of clinically depressed adolescents. The studies from Dopp ($N = 13$) and Hughes et al. ($N = 26$) being the only internationally published ones to our knowledge [24, 38]. They could show a reduction of depressive symptoms in partly supervised 12-week exercise interventions, with Hughes et al. comparing it to a stretching control condition [38]. One major issue addressed in the aforementioned studies is the difficulty to achieve adherence to an intensive exercise intervention, due to the marked lack of drive of depressive adolescents.

Aim of the present study

Summing up the state of science, there is a need of experimental studies investigating the effects of physical activity in clinically diagnosed depressed adolescents. Exercise treatment could be a viable add-on therapy for depressed adolescents who do not want or tolerate medication. A major barrier could be the difficulty to motivate depressed adolescents to intensive and high-frequency exercise interventions, especially with regard to endurance activities such as cycling or running. For this reason, in the study “Mood Vibes”, conducted from 2013 till 2015 at the Department of Child and Adolescent Psychiatry of the University Hospital of Cologne, whole body vibration (WBV) was chosen as an alternative exercising device. This kind of exercising can be performed on a high level of physical activity even

with a low motivation to exercise. Therefore, WBV could be a suitable alternative to gain anti-depressive effects of physical activity in depressive adolescents with a low urge to participate in cycling, running or other disciplines of regular sport therapy. We hypothesized that WBV would be as effective as endurance cycling in its clinical effects, measured by a decrease in depression scores in the Depressions Inventar für Kinder und Jugendliche (DIKJ) at weeks 6, 14 and 26 after inclusion. Secondly we hypothesized that exercise interventions would be superior to TAU. Included subjects were medication-naïve inpatient adolescents aged 13–18 with diagnosed major depression following DSM-IV-R/DSM-5 and ICD-10 criteria.

Procedures and measures

Study design

The study followed the design of a semi-randomized controlled trial. Intervention groups had to perform physical activity during 6 weeks for 3–5 days a week for 30 min, respectively. Participants were told to exercise 4 days weekly. The physical exercise was additional to treatment-as-usual (TAU). Participants were naïve to antidepressant medication. The control group received treatment-as-usual (TAU). Measurements were taken before intervention (t_0), after completing 6 weeks intervention (t_1) and then again at weeks 14 (t_2) and 26 (post t_2) (see Table 1) for all groups. Evaluation after week 26 consisted of questionnaires only. From week 6 on, add-on intervention was not continued. The intervention groups were randomly allocated to the vibration device or the stationary cycle condition (ergometer). Blinding was achieved only for the ratings done by the psychiatric care staff, as the main outcome-parameters were rated by the patients themselves. The study protocol was approved for the intervention by the University of Cologne Ethics Committee and has been officially registered in the German Clinical Trials Register in Freiburg under the identification DRKS00005120. The study was also supported by the Clinical Trials Center of the University of Cologne and registered in the official register of the University of Cologne. External monitoring according to protocol, good clinical practice, standard operating procedures and regulatory requirements was executed before and after the inclusion of the last patient (initiation and close-out visit).

Participant recruitment

Participants were drawn from three out of four inpatient units at the Department of Child and Adolescent Psychiatry Psychosomatic and Psychotherapy at the University Hospital of Cologne. Adolescents and parents were informed

Table 1 Study design

Screening		
Inpatient treatment		
Major depression		
DIKJ > 18 raw points		
No exclusion criteria		
Meeting inclusion criteria		
3 Measure points	Physical measures	Psychological parameters
t_0 = inclusion	Spiroergometry	Clinical interview (SKID-I)
t_1 = after 6 weeks intervention	including lactate blood levels	Depression questionnaires (DIKJ, SBB-DES, FBB-DES)
t_2 = 8 weeks after t_1 (without further intervention)	Jump mechanography	Sport questionnaires (EZK, WKV, MSES, etc.)
	Caliperometry, BMI	Borg Scale, diaries
1 Post-measurement		Depression questionnaires (DIKJ, SBB-DES, FBB-DES)
Post t_2 = 3 months after t_2 (without further intervention)		

about the existence of the study by flyers on the ward and on the internet page of the clinic. At admission to the inpatient treatment adolescents and parents were contacted by the study staff to inform about the possibility to participate in the program. If interested, adolescents were screened for eligibility. The participants were included consecutively.

Inclusion criteria

All participants (age 12–18 years.) were inpatients or day-clinic patients and had to meet DSM-IV/-5 and ICD-10 criteria of non-psychotic major depressive disorder (MDD), assessed by clinician rating with the Structured Clinical Interview for DSM-IV Axis I disorders, German version (SKID-I) [4, 77, 78]. Additionally, patients needed a baseline score in the “Depressionsinventar für Kinder und Jugendliche” (DIKJ) [72] of at least 18 raw points. They had to be of normal intelligence (i.e., IQ > 70 based on prior testing by Kaufman Assessment Battery for Children (K-ABC) [55] or Wechsler Intelligence Scale for Children (WISC)/Hamburg-Wechsler-Intelligenztest für Kinder (HAWIK) [61, 62]) and German language and reading were required as the assessment instruments were in German. Sport aptitude was assessed by the study physician. At baseline was performed a spiroergometry with electrocardiography (ECG) to assess maximal performance. The sport capacity was assessed following the official guidelines of the Society of Pediatric Sports Medicine (Gesellschaft für Pädiatrische Sportmedizin) [19]. Both genders were included. Comorbidities

were allowed as long as they were not part of the exclusion criteria.

Exclusion criteria

Adolescents were excluded when suffering from one of the following conditions: schizophrenia, other psychotic disorders or psychosis in the medical history, including psychotic depression, bipolar I and II disorder, personality disorders, pervasive developmental disorder or current substance abuse. A body mass index $< 16 \text{ kg/m}^2$, diseases causing restrictions to physical activity (e.g., insufficient gain of weight in eating disorders) and the use of vibration devices and ergometers or malignant diseases were also reasons for exclusion. Permanent psychiatric medication or medication with inherent psychotropic effects (anticonvulsants, steroids, methylphenidate, amphetamine, antidepressants, neuroleptics, benzodiazepines, mood-stabilizer), was not allowed. Intermittent PRN (pro re nata) medication was no reason for exclusion. We also excluded patients with Morbus Addison or non-substituted hypothyroidism.

Randomization

After screening for the inclusion criteria and written adolescent and parental (or legal guardians) consent to participate in the study, the principal investigator or a licensed study clinician conducted the Structured Clinical Interview for DSM-IV Axis I disorders, German version (SKID-I) to confirm diagnosis, check comorbidities for exclusion criteria, and evaluate current severity of the depressive disorder [78]. Randomization of vibration device and bicycle ergometer (1:1 ratio, permuted blocks of varying length) was implemented based on sealed, opaque envelopes by the Institute of Medical Statistics and Computational Biology of the University of Cologne (IMSB). The randomization sequence was generated using SPSS Statistics software (version 23; IBM Corp., Armonk, NY, USA). The adolescents willing to participate in the measurements but not in the physical activity intervention were recruited for the Treatment As Usual (TAU) group.

Primary and secondary outcome measures

Depressionsinventar für Kinder und Jugendliche (Depression Inventory for Children and Adolescents)

The German “Depressionsinventar für Kinder und Jugendliche” (DIKJ) was used as primary outcome measure for depression. The DIKJ is a self-report questionnaire assessing the severity of depressive symptoms in children and adolescents as of grade two, conceived on the basis of the

anglosaxon children’s depression inventory (CDI) [45]. All fundamental symptoms of depression are assessed and formulated in a suitable way for children according to the criteria of major depression in the DSM-IV. Furthermore, typical accompaniments and impacts of depression are captured. Using unselected student samples Stiensmeier, Schürmann and Duda (1989) found an internal consistency between $0.85 > \alpha \geq 0.82$ with a tendency for higher statistical values in older age samples [72]. In clinically conspicuous children and adolescents the internal consistency lies at $\alpha \geq 0.91$. Additionally, different studies demonstrate good discriminant and convergent validity [72]. A raw-score of 18 was set as cut-off criteria for inclusion into the study.

Structured interview for DSM-IV

Clinical rating of depression and assessment of comorbid disorders was performed using the German version of the Structured Clinical Interview for DSM-IV “Strukturiertes Klinisches Interview für DSM-IV” (SKID-I). The SKID-I serves to determine and diagnose psychic syndromes and disorders based on definitions of Axis I disorders within the DSM-IV (2000) 4th ed., it is a structured interview lasting approximately 60 min [78].

Youth Self-Report (YSR 11-18) and Child Behavior Checklist (CBCL 6-18)

The Child Behavior Checklist (CBCL), completed by parents, and the Youth Self-Report (YSR), completed by adolescents, form part of the Achenbach System of Empirically Based Assessment (ASEBA) for school-age children [2, 3, 23]. The questionnaires are based on factor analyses coordinated across the forms. Both comprise a part covering social competence and adaptive functioning and another part assessing behavioral problems. The 118 items assessing the behavioral problems provide scores for eight narrow-band scales or syndromes (anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior), and three broad-band scales (internalizing behavior problems, externalizing behavior problems, and total behavior problems). Raw scores are transformed into *t*-scores to allow comparison with children from the same gender and age. The *T*-score cut-offs categorize the subjects into clinically, borderline or not-clinically conspicuous.

Diagnostic system for mental disorders in childhood and adolescence (DISYPS-II)

The diagnostic system for mental disorders in childhood and adolescence (DISYPS-II) is based on the international

classification systems ICD-10 and DSM-IV. It includes diagnostic checklists for clinician rating (Diagnose Checkliste—DCL), evaluation forms for parents or other thirds (Fremdbeurteilungsbögen—FBB) and self-rating forms (Selbstbeurteilungsbogen—SBB). It covers seven psychiatric conditions (ADHD, conduct disorder, anxiety and obsessive compulsive disorders, depression, pervasive developmental disorder, bonding disorders and mutism, tic disorder). The questionnaire for diagnosis of depression comprises 29 items representing symptom criteria from ICD-10 and DSM-IV, as well as 8 competence items. The FBB–DES was rated by parents and blinded professional personal (nurses and educators) from the ward.

Magglinger Sports Enjoyment Scale (MSES) and self-designed feed-back questionnaire

The MSES was constructed on the basis of the English PACES questionnaire (Physical Activity Enjoyment Scale) from Kendzierski et al. and the German Befindlichkeitsskalen (BFS; State Scale) from Abele and Brehm [1, 44, 56]. It comprises 20 items on five scales (perceived competence, social interaction, specific experience of movements, enjoyment of activity, positive interaction with trainer). The items are rated on a 7-point Likert scale. In non-clinical samples its internal consistency is stated between *Cronbach's alpha* $0.95 > \alpha \geq 0.75$.

The self-designed feed-back questionnaire from our working group comprised 12 closed-ended questions rating the acceptance and critics of the exercise interventions and the subjective motivations of the participants. Rating was possible on a 4-point scale with 0 = never/not at all and 3 = completely right/always. Additionally, subjects could fill in three open questions with regard to the program.

Methods regarding secondary outcome parameters not subject to the present article

Aside from the above-mentioned questionnaires, the adolescents completed the following sport specific forms: Eigenzustandsskala (EZK; Inherent State Scale), Wahrgenommene Körperliche Verfassung (WKV; Perceived Corporal State), Motivation und Hemmnisse in Bezug auf Sport (Motivational Factors and Barriers in Sports), a modified Borg Scale (Rating of Perceived Exertion).

Physical examination and measurements

Participants included into the study performed the following physical examinations before starting the intervention (t_0), after 6 weeks intervention (t_1) and after 8 weeks without exercise intervention (t_2): spiroergometry (using systems ZAN[®], Blue Cherry and ergometer-cycle ergoline[®]) with

electrocardiography (AMEDTEC ECG pro[®]), including measuring of lactate in blood gas analysis, VO₂ (maximal aerobic capacity), VE (respiratory minute volume), RER (respiratory quotient), HR (heart rate), RR (arterial blood pressure), assessing the maximal watts per kilogram; caliperometry (standardized estimation of bodyfat by skinfold caliper Siber-Hegner[®] measuring scapula and triceps skinfolds of left body side; anthropometric measurements (height, weight, body mass index (BMI), determined using clinical standard stadiometer and digital electronic scales; mechanography assessing peak jump force (PJF), and peak jump power (PJP), with the Leonardo[®] Jumping Platform (Novotec GmbH, Pforzheim, Germany).

Body weight was measured by the nurse staff at admission in the inpatient ward to the nearest 0.1 kg in underwear using a digital scale. Body height was measured using a wall-mounted stadiometer to the nearest 0.1 cm. Measurements were taken from the clinical file documents. Calculation of BMI was done by the formula $BMI = \text{bodyweight (kg)}/\text{height (m)}^2$. BMI percentiles were determined following Kromeyer-Hauschild curves [46]. Calipometry was done with hanging arm on the left body side. Three measurements by the same examiner were taken to calculate mean for each measurement. Spiroergometry was done according to the German spiroergometry guidelines [74]. Cycling started without wattage load for 2 min and was then increased with 25 W every 2 min. The following parameters were calculated and recorded electronically: wattage (W), heart rate (HR/min.), blood pressure (RR in mm Hg), oxygen uptake (VO₂ l/min), carbon dioxide output (VCO₂ l/min), external lung respiration (RER as VCO₂/VO₂), respiratory minute volume (VE l/min) and oxygen saturation (SP O₂ in %). Lactate was analyzed in the German Sports University Cologne (Deutsche Sporthochschule Köln) in the Department of Sportsmedicine, using lactate-analyzer of EKF Diagnostics[®]. Mechanography testing was done according to Novotec[®] handbook instructions [32, 76]. Participants performed the program *Single Two Leg Jump* three times, then the best performance defined using best EFI (Esslinger Fitness Index) was included in the data analysis.

Intervention

Training procedures

After being randomized to the intervention groups the training took place daily from 5 to 6 p.m. in the training facilities of the UniReha GmbH, Pediatric Rehabilitation Center, (rehabilitation and physiotherapy training rooms of the University Hospital of Cologne). It was supervised by two members of the study staff controlling for correct execution of the physical activities. The group size differed constantly (ergometer range 1–6, WBV range 1–4) as the participants

were included consecutively. Participants could choose one free day weekly and exceptionally two free days, if in the whole 6 weeks the number of trainings equaled 18 sessions.

Vibration plate

The whole body vibration training (WBV) was executed on the Galileo® training device (model Advanced Plus) from Novotec Medical GmbH. The vibration plate stimulates a movement pattern similar to human gait. The training principle is based on the activation of proprioceptive spinal circuits, inducing a certain number of stretch reflex contractions per second depending of the frequency chosen. The training improves muscle power and function and coordination of the legs and the hip and also partly of the trunk, having only a small effect on the cardiovascular system. Besides that it improves bone formation and the metabolism in skeletal muscles and skin [69]. It is used in rehabilitation and training in different areas, one pilot study covering therapy of stereotypies in autism [11, 29, 31, 69, 70]. The side-alternating vibrations generated by Galileo® can be continuously varied in amplitude and frequency and the training load is determined by those parameters. The adolescents of the WBV group were trained at a frequency of 20 Hz and an amplitude of 2 mm. The first 12 days the length of the 6 exercises on the plate was of 2 min, and the following sessions of 3 min with an equal pausing time in between, necessary for the recovery of the muscle strength. This means that only by WBV technique the same number of muscle contractions as walking a distance of 15.840 steps in the first 12 days and 23.760 steps in the following sessions was executed. Additionally, the 6 standardized exercises on the plate comprised contractions of the arms and shoulder, rotation of the trunk, varieties of leg positions and squats (Fig. A1).

Ergometer training

The ergometer training took place in a group room in Unireha® GmbH on stationary cycles from the firm Ergosana® and was supervised by the study personnel. In cooperation with the Deutsche Sporthochschule Köln (German Sport University Cologne) a 30-min interval training calculated on the maximal performance in the previous spiroergometry results was applied (Fig. A1). The fulfillment was supervised by the training staff.

Treatment as usual (TAU)

Participants in the treatment as usual condition followed their therapy schedule at the inpatient units of the Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy of the University Hospital of Cologne.

Common therapy offers were psychotherapy in form of individual sessions with a psychotherapist or psychiatrist, group psychotherapy sessions, exercise therapy, art therapy and music therapy. The intervention groups received TAU plus ergometer or WBV intervention.

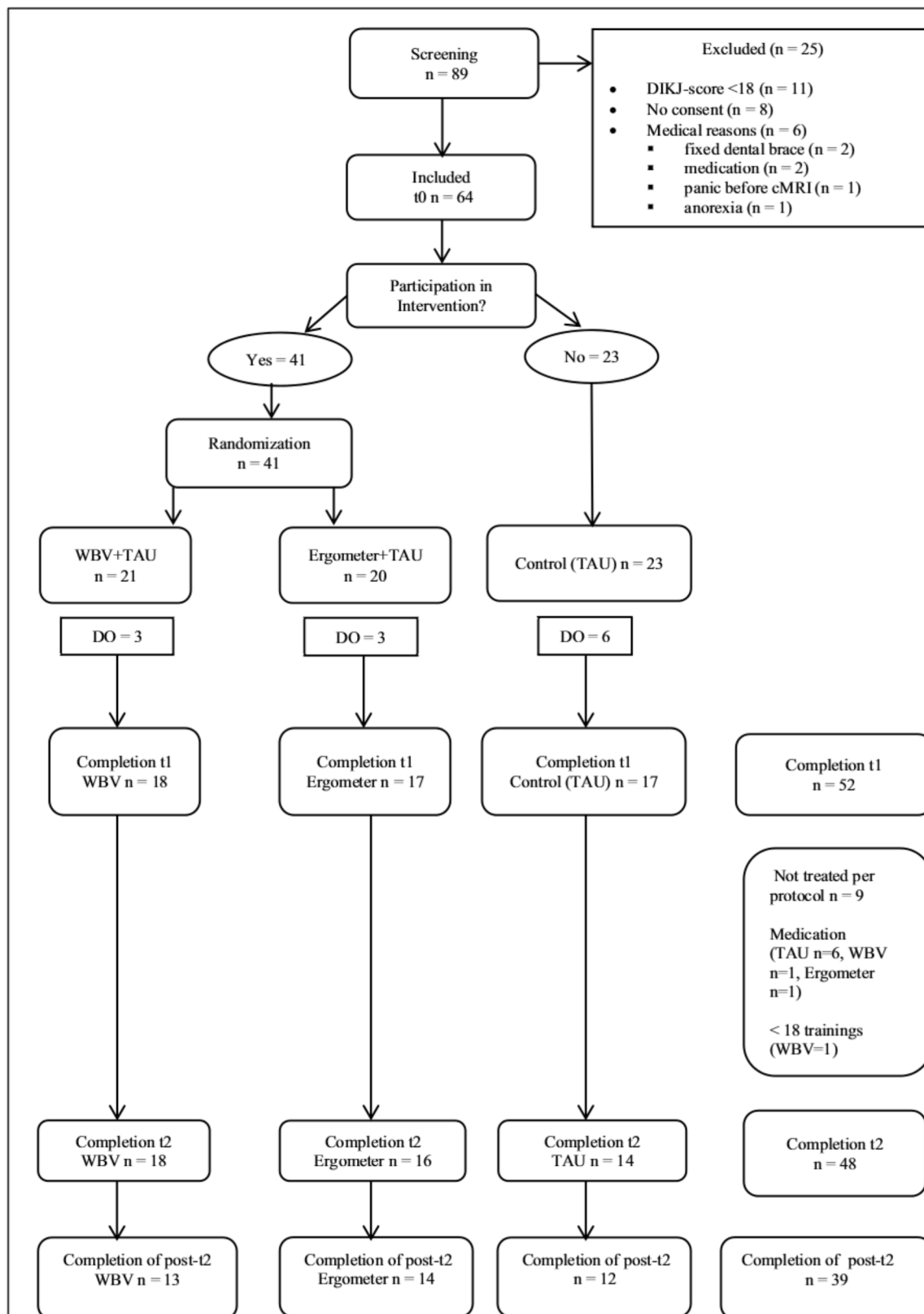
Statistical analysis

Analysis was done according to the (modified) intention-to-treat (ITT), i.e., including all randomized patients with at least two valid assessments and having participated in at least one training session. Subjects with medication started during the study and administered for longer than 3 weeks were also considered ITT. Patient data were summarized using count (percentage), mean $\pm$ standard deviation (SD) or median (interquartile range (IQR)), contingent on distributional characteristics. Normality of empirical distributions was formally evaluated by the Shapiro–Wilk test (at 10% significance level). A mixed model for repeated measures (MMRM) approach was taken for the primary endpoint, DIKJ score value, with fixed effects for treatment, time, sex, age and the interaction treatment*time (type III sums of squares, ARH1 covariance structure over time). Missing values were not imputed. Pairwise contrasts of estimated marginal means were computed. Effect size estimates (Cohen's *d*) with 95% confidence intervals were derived from these contrasts. Potentially confounding variables were evaluated in a stepwise manner (in- and exclusion from the model equation). Secondary endpoints, BDI II, SBB and FBB, were analyzed along the same lines. Differences in remission and drop-out rate between the treatment groups at each time point were assessed by means of Fisher's exact test. All reported p-values are two-sided and considered statistically significant if $\leq 5\%$. All calculations were done with SPSS Statistics software (version 23; IBM Corp., Armonk, NY, USA).

Results

Subjects included

89 subjects were screened continuously over a 2-year period in the inpatient and day-clinic department of our child and adolescent psychiatry. 64 patients met criteria for study eligibility (see Fig. 1). From the excluded $n = 11$ had a DIKJ score < 18 , $n = 8$ did not give consent, $n = 6$ were excluded for medical reasons (dental brace, psychotropic medication, BMI $< 16 \text{ kg/m}^2$). In the course of the study 41 participants were randomized to the intervention conditions, whereas 23 were included in the treatment-as-usual (TAU) control condition (Fig. 1).

**Fig. 1** Flow chart: participant enrolment and dropout

Dropouts over time

Dropouts were defined as the subjects not participating in $t1$ (second assessment of measurements). Of 64 participants included in the study, 12 dropped out prior to $t1$ (ergometer = 3, WBV = 3, control = 6; $p = 0.565$). Most patients who dropped out were either released from their inpatient treatment at the hospital or had no motivation to complete the tests at $t1$. The total number of participants at $t2$ was 48 (ergometer = 16, WBV = 18, control = 14) and 39 at follow-up (post $t2$: ergometer = 14, WBV = 13, control = 12). However, some questionnaires within all conditions could not be included in the analysis as they were either not completed or not handed in.

Demographic and clinical characteristics at baseline

18 boys (28.1%) participated in the study (see Table 2). 89.1% of the total sample were inpatients, 10.9% received day-clinic treatment. Mean age was 15.9 ± 1.15 years, IQ assessed by WISC IV (Wechsler Intelligence Scale for Children) with 100.12 ± 11.94 in the average. BMI was with 24.6 ± 6.2 kg/m² and BMI percentile 68.3 ± 31.9 ranging

between normal and overweight. The most frequent comorbidities in the sample were anxiety ($n = 14$ [21.9%]) and somatoform disorders ($n = 8$ [12.5%]), without significant group differences (Table A3). The group differences between the mean scores at baseline of the depression questionnaire (DIKJ) were also found to be not statistically significant with 27.6 ± 6.4 DIKJ score for the total sample (see Table 2). In the total sample $n = 15$ (26.3%) were member in a sports club and 17 (29.8%) performed regular sports for > 2 times a week. TV time and PC time amounted to 98 ± 129 and 89 ± 141 min daily. $n = 17$ were smoking, $n = 16$ were consuming alcohol sporadically. $n = 3$ reported having already tried Ecstasy and consuming Cannabis before admission. $n = 20$ (44.4%) of the sample had psychiatric diagnosed parents, the divorce rate was 60.9%. In contrast to “parental divorce” and “PC time”, the data concerning history of substance abuse, leisure time activities and regular sports practice in day-to-day life did not show statistically differences between the groups. Psychiatric comorbidities were diagnosed in 28% of the participants. Anxiety disorders were the most frequent diseases. There were trends for increased anxiety disorders in the participants with ergometer training and less somatoform disorders in the control group.

Table 2 Demographic and clinical characteristics at $t0$

	Subjects												<i>p</i> values
	Total <i>N</i> = 64			Ergometer <i>n</i> = 20			WBV <i>n</i> = 21			Controls <i>n</i> = 23			
Sex ♂	18	(28.1)		8	(40)		6	(28.6)		4	(17.4)		0.268
Age	15.9	± 1.1		16.1	± 1.2		15.9	± 1.2		15.7	± 1.1		0.531
BMI	24.6	± 6.2		26	± 7.6		24.7	± 5.9		23.3	± 5.0		0.361
BMI percentile	68.3	± 31.9		69.6	± 34.9		69.5	± 30.7		66.2	± 31.8		0.942
IQ	100.1	± 11.9	(4)	100.4	± 8.4	(1)	100.4	± 14.1	(1)	99.6	± 13.0	(2)	0.968
DIKJ score	27.6	± 6.4		27.0	± 6.2		26.9	± 6.2		28.8	± 6.9		0.560
Setting													
Inpatient	57	(89.1)		19	(95)		18	(85.7)		20	(87)		0.686
Day-clinic	7	(10.9)		1	(5)		3	(14.3)		3	(13)		0.686
Length of stay	68	± 33		80	±36		60	± 20		64	± 39		0.123
Psychiatric diagnosed parent	25	(46.3)	(10)	9	(50)	(2)	9	(50)	(3)	7	(38.9)	(5)	0.834
Parents divorced	28	(43.8)		14	(70)		9	(42.9)		5	(21.7)		0.044
Sports club member	15	(26.3)	(7)	7	(36.8)	(1)	3	(15.8)	(2)	5	(26.3)	(4)	0.396
Regular sports (> 2 times/week)	17	(29.8)	(7)	7	(36.8)	(1)	6	(31.6)	(2)	4	(21.1)	(4)	0.702
TV time (minutes/day)	107	± 133	(7)	133	± 146	(2)	117	± 168	(2)	74	± 71	(3)	0.371
PC time (minutes/day)	90	± 142	(14)	163	± 219	(5)	75	± 90	(4)	43	± 61	(5)	0.044
Smoking	17	(29.3)	(6)	6	(31.6)	(1)	7	(36.8)	(2)	4	(20)	(3)	0.514
Alcohol	16	(27.6)	(6)	5	(26.3)	(1)	8	(42.1)	(2)	3	(15)	(3)	0.171
Cannabis (> 1/week)	3	(5.2)	(6)	2	(10.5)	(1)	1	(5.3)	(2)	0	0	(3)	0.310
Ecstasy (sporadic)	3	(5.2)	(6)	1	(5.3)	(1)	2	(10.5)	(2)	0	0	(3)	0.310
Speed (sporadic)	1	(1.7)	(6)	0	0	(1)	1	(5.3)	(2)	0	0	(3)	0.655

Quantitative variables are summarized as mean $\pm$ SD (missing), *p* from one-way ANOVA; qualitative variables as *n* (%), *p* from Fisher's exact test

Adherence to sports program and additional sports therapy time

The number of trainings in the 6 weeks of intervention did not differ significantly with 23.5 ± 2.5 interventions for the ergometer condition and 22.1 ± 3.70 interventions for the WBV group. The maximum number of trainings was 28 and 27, respectively. So the medium number of trainings was approximately 4 times/week. The number of trainings introduced as a covariate in the mixed model analysis did not show to have an effect. Nevertheless, some trend could be seen when clustering the groups in 19–21 trainings, 22–24 trainings and 25–28 trainings. Here the high-frequency group showed a statistical trend in the pairwise comparisons (Table A6). The self-reported additional sports practice diary was only filled in by $n = 7$ for the ergometer group and $n = 6$ for the WBV group. The control condition did not hand it in at all. The total sports therapy time in minutes/week documented in the clinical files from each patient was summarized for weeks 1–6 (ergometer = 256 ± 258 ; WBV = 161 ± 171 ; Control = 308 ± 339) and weeks 7–14 (ergometer = 117 ± 227 , WBV = 42 ± 66 , Control = 134 ± 212) and introduced in the mixed model analysis. It showed no statistically significant influence.

Motivation

Motivation with regard to the fulfilled physical activity was assessed by the Magglinger Sports Enjoyment Scale (MSES) and the self-designed feed-back form (Tables A11–A13). In the MSES subscale “Enjoyment” (Liked the activity, Fun, Joy, Living Good Moments), the question “Fun” was rated statistically higher from the ergometer group compared to WBV, whereas the questions “liking the activity”, “joy” and “living good moments” showed no significant group difference. Sumscore group differences of the Enjoyment Scale were also not statistically different. For the Scales “Perceived Competence” and “Specific Movement Experience” ergometer was rated higher compared to WBV. On the other hand, in the self-designed feed-back questionnaire the question “Liked physical activity” was rated higher by WBV and “Would have preferred the other intervention” was rated in the mean 0.55 and 0.58, respectively, for ergometer and WBV (0 = never/not at all and 3 = always/completely true). Training frequency (4 times/week) was not perceived as too intensive (mean = 0.55 ergometer group and 0.42 for WBV group) neither as too long per unit (mean = 0.45 for ergometer group and 0.33 for WBV group). The motivation due to trainers was perceived as high in both groups (mean = 2.55 for ergometer group and 2.42 for WBV group). “Would recommend it to others” was rated a little higher from ergometer group, whereas “Got motivated to continue exercise” was rated higher by WBV group (see Table A12).

MSES subscales introduced in the mixed model analysis showed no statistically difference.

Adverse events

Neither adverse events (AE) nor serious adverse events (SAE) with relationship to the intervention were reported. From the intervention groups one subject suffered a metacarpal fracture due to self-injury but continued trainings. One subject suffered a skin infection, but also continued exercising. One subject was moved to the closed ward because of elevated suicidality for a short crisis not connected to the trainings and could also continue exercising.

Total therapy times comprising TAU and length of stay

The therapies comprising TAU were quantified for each patient by summing up the total minutes of every therapy form offered in the ward (psychotherapy, group therapy, arts therapy, sports therapy, music therapy, social work interventions). Total psychotherapy in minutes weeks 1–6 was almost equal in all groups (mean = 311 ± 173). In weeks 7–14 it was the highest in ergometer group with mean = 190 ± 243 and mean = 71 ± 105 for WBV and mean = 70 ± 104 for control group (Table A5). Group differences were here almost statistically significant with $p = 0.06$. Nevertheless, total therapy times included as covariates in mixed model analysis showed no significant influence and the differences in length of stay have to be taken into account. Sports therapy comprising TAU was highest in control group with mean = 308 ± 339 min in weeks 1–6 (for ergometer group = 256 ± 258 and WBV = 161 ± 171). Also in weeks 7–14 control group got the highest amount of sports therapy in minutes with mean = 134 ± 212 (ergometer group = 117 ± 227 and WBV = 42 ± 66). Nevertheless, the differences between groups were not statistically significant (Table A5). Same can be reported for the medium length of stay which was 68 ± 33 days for the entire sample.

Medication

Patients were supposed to be medication naïve. Those who nevertheless received medication with psychotropic effects in the course of the study for longer than 3 weeks, were treated as ITT. The medication given was in decreasing prevalence: SSRI (fluoxetine, sertraline, citalopram), antipsychotics (tiapridex, olanzapine), sedatives (promethazine, lorazepam), stimulants (methylphenidate). 47 subjects (73.4%) were medication naïve, 9 received PRN for not longer than 3 weeks and 8 received medication for longer than 3 weeks (Table A2). There was a trend for more permanent medication in the control group. Medication introduced

in the mixed model analysis showed no statistically significant influence.

Evolution of anthropometric data and sporting performance

In weeks 1–6 of the study BMI percentiles and body fat measured by calipometry did not decrease for the intervention groups (see Table A8 and A10). The cardiopulmonary effects measured by spiroergometry (maximal performance in wattage, VO_2 peak/kg) improved for the cycling condition but not for the WBV group. Same could be seen for the performance in the mechanography (jump performance in wattage/kg) (see Table A7 and A9). Introduced in mixed model analysis, BMI, calipometry, performance in wattage, RER and jump peak force showed to have no statistically significant influence on the DIKJ outcomes.

Effect of treatment measured by DIKJ (primary endpoint)

Mean DIKJ scores (Fig. 2) were decreasing for the ergometer and WBV condition from 27 at baseline to 21.8 after 6 weeks intervention, to 18.3 and 20.3 after 14 weeks and were shown to be under the cut-off for clinical depression at follow-up (14.3 and 13.6). The DIKJ score from the control condition stayed almost equal with 28.8 at baseline and 28.6 after 6 weeks. At week 14 the control condition reached 22.9 and at follow-up 23.6 (Table 3).

The mixed model showed statistical significance for time and sex with women having higher DIKJ scores. The pairwise comparisons was statistically significant for the intervention conditions compared to controls at week 26 ($F = 3.0$, $df = 39.1$, $p = 0.037$ for the ergometer condition and $F = 3.0$, $df = 39.1$, $p = 0.042$ for the WBV condition), showing a trend at week 6 ($F = 1.7$, $df = 58.9$, $p = 0.082$ for WBV and $F = 1.7$, $df = 59.7$, $p = 0.19$ for the ergometer condition, see Table 4). Differences in DIKJ scores between active interventions are not statistically significant at any time point (see Table 4 for details). None of the variables medication, number of trainings, therapy times, length of stay, additional sports, and BMI seemed to act as confounder (Table 4). The calculated effect sizes (Cohen's d) after 6 weeks were 0.45 for the ergometer condition and 0.60 for the WBV condition, after 26 weeks 0.85 and 0.85, respectively (Table A4). Reduction of symptoms calculated on DIKJ scores < 18 were after 6 weeks 29.4% in the ergometer group, 50.0% in the WBV group and 17.6% in TAU. After 14 weeks 57.1% in ergometer and 40.0% in WBV compared to 28.6% in controls. After week 26, remission rates were 71.4% for ergometer, 61.5% for WBV and 25.0% for controls (Table 3). The two intervention groups together, remission rates of symptoms were 40.0% at t_1 , 48.3% at t_2 and 66.7% after week 26. Remission rates do not differ statistically significant between the three groups at every time point. Intervention groups together compared to control show significant difference in remission rates after week 26 only ($p = 0.035$).

Fig. 2 Mean-DIKJ Rawscore mixed model analysis

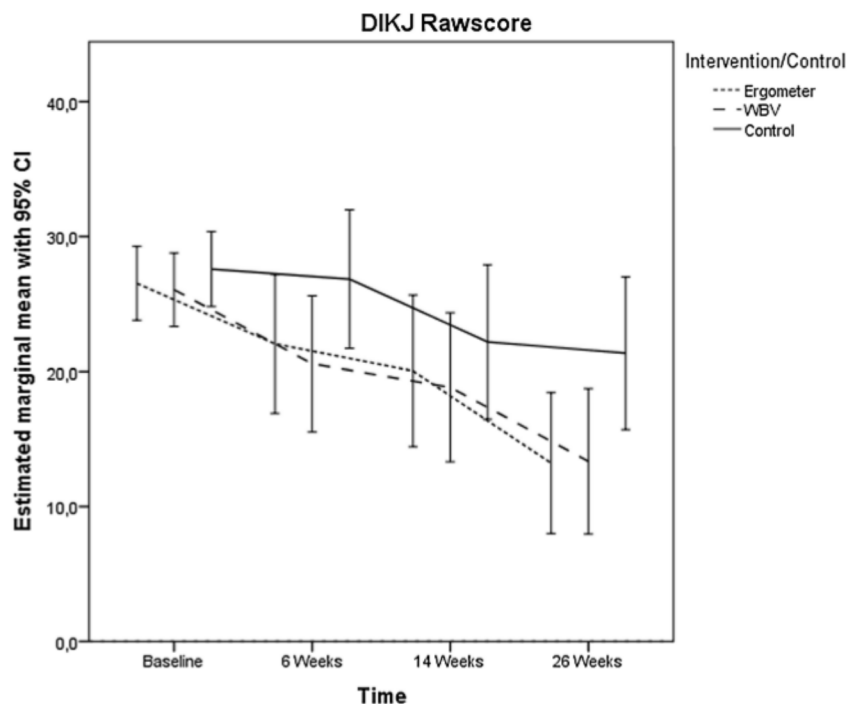


Table 3 DIKJ Rawscore (Min., Max., Mean)

	<i>N</i>	Mean	SD	Min.	Max.	<i>N</i> = DIKJ < 18 (remission rate)
Baseline						
Ergometer	20	27.0	6.2	18	39	0
WBV	21	27.0	6.2	18	40	0
Control	22	28.8	6.9	18	39	0
6 weeks						
Ergometer	17	21.8	10.3	6	45	5 (29.4)
WBV	18	21.8	13.3	4	46	9 (50)
Control	17	28.6	10.8	5	44	3 (17.6)
14 weeks						
Ergometer	14	18.3	10.4	3	33	8 (57.1)
WBV	15	20.3	11.9	1	42	6 (40)
Control	14	22.9	11.1	2	35	4 (28.6)
26 weeks						
Ergometer	14	14.3	7.2	3	26	10 (71.4)
WBV	13	13.6	7.8	0	24	8 (61.5)
Control	12	23.6	12.4	2	43	3 (25)

SD standard deviation, *Min.* minimum, *Max* maximum (%)

Effect of treatment measured by SBB–DES and FBB–DES (secondary endpoint)

Self-rating SBB–DES showed equivalent to DIKJ faster and stronger decrease of scores in the intervention groups getting statistically significant in the pairwise comparisons for WBV group compared to TAU after week 26 (Fig. 3 and Table A15). Only the intervention groups were under the clinical cut-off after week 26 with a mean sum-score of 0.76 for ergometer group and 0.52 for WBV group compared to 1.03 for TAU. Parents rating showed lowest sum-scores after week 14 with mean = 0.68 for the ergometer group and mean = 0.59 for the WBV group compared to mean = 1.11 for TAU condition (Fig. 4). After 26 weeks scores reached 0.64 for ergometer, 0.67 for WBV and 0.99 for control group (Fig. 4). In pairwise comparisons in the mixed model analysis significance at week 14 was $F = 2.6$, $df = 23.0$, $p = 0.049$ for WBV compared to control and a trend for ergometer with $F = 2.6$, $df = 22.3$, $p = 0.093$. Rating from blinded psychiatric care staff was lowest for WBV group at week 14 with mean = 0.31 yet not statistically significant compared to control (mean = 0.62; $F = 2.5$, $df = 25.5$, $p = 0.096$; see Table A17). Introduced in the mixed model analysis none of the variables medication, number of trainings, therapy times, length of stay, additional sports, and BMI seemed to act as confounder.

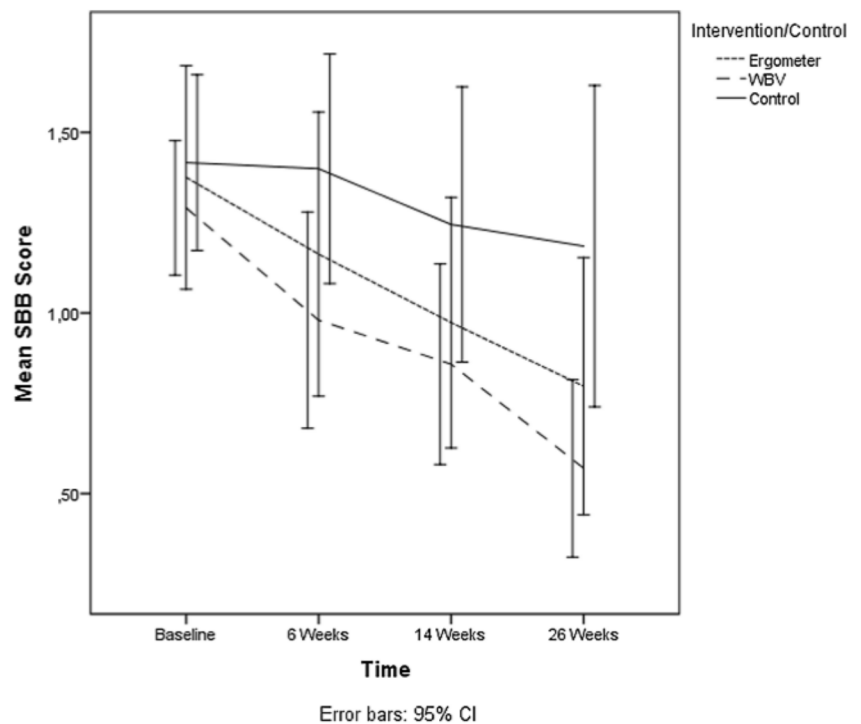
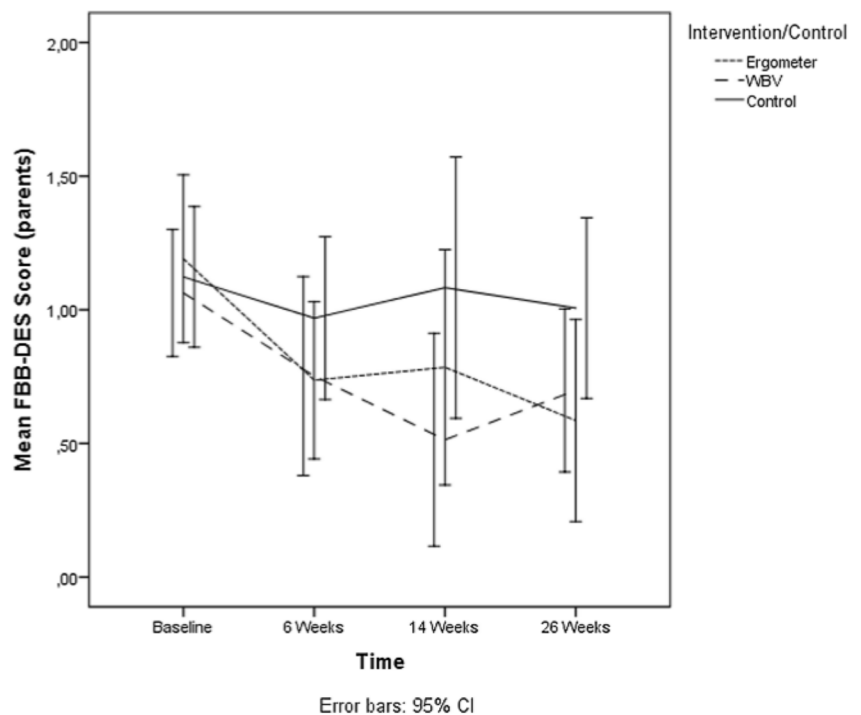
Discussion

In the study “Mood Vibes” we investigated the feasibility and effectiveness of a high-frequency whole body vibration (WBV) training as add-on anti-depressive treatment in medication-naïve inpatient adolescents with diagnosed major depression in comparison to an endurance cycling condition. Based on the existing literature, we hypothesized that both exercise interventions would be superior to TAU [24, 38, 47, 57]. WBV training was chosen because of its intensive muscular training effects demonstrated in previous studies, combined with a low necessity of active participation [11, 15, 69]. Considering the lack of activation and urge to practice in depressed adolescents as an inherent characteristic of major depression diagnosis, we argued that exercise interventions with active endurance training may be too demanding for some of the patients as discussed in prior studies [13, 65, 67]. Especially in the beginning of treatment, when depressive symptoms are most intense, more passive training could be suitable if the effects would be comparable to more active exercising [13, 34]. In our results we found that adherence and drop-out rates were equal in both exercise groups, so feasibility could be demonstrated for both interventions. This is in line with the formerly published trials of Dopp et al. and Hughes et al. [24, 38]. In difference to our program, in those studies, participants had to perform 3 times weekly and there was a monetary reward

Table 4 Pairwise comparisons and effect sizes DIKJ score intervention/control

Time	Pairwise comparisons									
	(I) Intervention/control	(J) Intervention/control	Mean difference (J–I)	Std. error	<i>F</i>	<i>df</i>	Sig.	95% Confidence interval for difference		Effect size <i>d</i>
								Lower bound	Upper bound	
Baseline	Control	Ergometer	–1.1	1.9	0.4	64.9	0.584	–2.8	4.9	–0.17
		WBV	–1.5	1.9	0.4	64.6	0.415	–2.2	5.2	–0.25
	Ergometer	WBV	0.5	1.9	0.4	64.5	0.805	–3.3	4.3	0.08
6 weeks (<i>t1</i>)	Control	Ergometer	–4.8	3.6	1.7	59.7	0.190	–2.4	12.0	–0.45
		WBV	–6.3	3.6	1.7	58.9	0.082	–0.8	13.4	–0.60
	Ergometer	WBV	1.5	3.6	1.7	57.6	0.681	–5.7	8.6	0.14
14 weeks (<i>t2</i>)	Control	Ergometer	–2.1	4.0	0.4	47.3	0.592	–5.8	10.1	–0.20
		WBV	–3.4	3.9	0.4	46.2	0.395	–4.5	11.2	–0.32
	Ergometer	WBV	1.2	3.9	0.4	45.9	0.757	–6.6	9.0	0.12
26 weeks (post- <i>t2</i>)	Control	Ergometer	–8.1	3.8	3.0	39.1	0.037*	0.5	15.8	–0.85
		WBV	–8.0	3.8	3.0	39.1	0.042*	0.3	15.7	–0.84
	Ergometer	WBV	–0.129	3.7	3.0	38.2	0.972	–7.6	7.3	–0.01

Based on estimated marginal means and the mean difference is significant at the 0.05 level; dependent variable: DIKJ score

Fig. 3 SBB–DES score**Fig. 4** FBB–DES score parents rating

influencing attendance. Both studies were performed with outpatient individuals, so adherence could be more difficult for logistic reasons. On the other hand, depressive individuals in outpatient treatment are normally more active than those requiring inpatient treatment.

As hypothesized, the anti-depressive effects of WBV training showed to be comparable to the endurance cycling

condition. With regard to the primary endpoint (clinical depression measured by DIKJ score) both interventions showed quicker decrease in symptom severity, with a statistical trend for WBV after 6 weeks. After week 26, reduction in depression scores was significant in both interventions compared to TAU ($d = -0.85$ (95% CI -1.64 to -0.05) for ergometer and $d = -0.84$ (95% CI -1.65 to

–0.03) for WBV). In addition to the earlier response, only the intervention conditions showed remission after week 26 with mean DIKJ scores = 14.3 for ergometer and 13.6 for WBV group, whereas control condition stagnated with mean DIKJ scores of 23.6 after week 26. Remission rates calculated on DIKJ scores < 18 for the two intervention groups together, were 39.7% after week 6, 48.6% after week 14 and 66% after week 26. So as hypothesized, the easy-to-perform WBV muscular training showed similar effects to the more activity demanding cycling program. With regard to effect sizes and remission rates in randomized SSRI trials on adolescents, the present findings of this partly randomized study allow the assumption not to be inferior to a combination treatment of CBT and fluoxetine [26, 27, 50]. Thereby, the latter are largely conducted in outpatient settings, potentially with patients who are less severely affected.

It is a major issue in the anti-depressive effects of physical exercise to differentiate the influence of psychological factors (like e.g., intrinsic and extrinsic motivations, social factors, increased attention through trainers, etc.) from the pure biological effects generated by physical activity in the neurobiological sense. In the studies of Dopp and Hughes, participants could creatively design their independent sessions (2 out of 3 weekly) [24, 38]. So the approach depended on psychological factors (e.g., enjoyment, sense of achievement), considered as most important by some studies, compared to our more functional concept [13, 21, 34]. We tried to assess the psychological influences using self-designed feedback forms and standardized questionnaires like the Magglinger Sports Enjoyment Scale (MSES). In sum, the factors “perceived competence”, “intrinsic movement experiences”, “social interaction in the group”, “interaction with the trainer” or “intrinsic enjoyment” did not seem to act as confounders. The feedback form showed nevertheless that motivation through the trainers seemed to be an issue. This factor should be investigated in future experiments, introducing a placebo-exercise group to hold apart physiological from psychological influences. With regard to the satisfaction of the program itself, the specific activities were liked by the patients, with a small advantage for WBV. The WBV group got (almost significantly) more motivated to continue exercising after the program than the cycling group, whereas the ergometer group perceived more positive changes on the general body feeling than WBV. This finding is quite interesting, as we expected that improved body perception would be transmitted more by WBV muscular training than by the cycling intervention. On the other hand, it is to note that the motivation to continue exercising after discharge is more elevated after WBV training, so this training form seems to be imaginable for adolescents in daily routine. This finding is important as the motivation for active exercise such as cycling or running could even be more difficult to

achieve in non-supervised trainings after demission, due to the condition itself [5].

With regard to the exercise interventions chosen by Dopp and Hughes it must be noted that subjects were allowed to select an activity they liked personally, so the influences of subjective motivation and well-being in the practice of the activity were certainly a lot higher [24, 38]. In adult studies the discussion which exercise intervention in which setting and intensity would be most effective, was recently again addressed in a meta-analysis [71]. The author’s conclusion was, that aerobic exercise, either in group or individually, with some level of supervision and at a moderate intensity for three times weekly and at least 9 weeks, would be most effective, contrasting with the NICE guidelines. The latter go further, recommending 10–14 weeks training and a duration of 45–60 min [60, 71]. With regard to adolescents, e.g., the Australian guidelines recommend 60 min medium to vigorous physical activity for 3–5 times/week and recommendations of the World Health Organization (WHO) amount to 60 min moderate to vigorous activity daily [54, 58]. Our findings are somewhat different and lead to the conclusion that an activity performed for only 30 min 4 times weekly over 6 weeks, either in group or individually and either muscular or cardiovascular training, may have the same positive effects. As stated before, introduced in our mixed model analysis as a covariate, the number of trainings (between 18 and 30 possible sessions) seemed to have no influence on the outcome. Although in the cluster analysis, the group with 25–28 trainings (i.e., 4–5/week), showed the greatest effects in reduction of DIKJ scores, but not to a statistically significant extent (Table A6). Our findings are interesting because the shorter the needed exercise therapy is to become effective, the easier it will be to motivate adolescents to train. Secondly, it is interesting that the effect of physical activity seemed to act as a booster: once the 6 weeks intensive exercise is completed, the intervention groups continued to improve in their clinical outcome. This is especially attractive with regard to the WBV condition. As it is easy to perform also for listless individuals, it could be used as a “bridging”-technique when more active exercising is still not possible due to the depressive condition. Further on, when clinical depression is less severe, more active physical activity could be introduced. In a second step, the patient could then choose the type of intervention suited personally to continue exercising in day-to-day life (e.g., varying individual or group exercise, outdoor or indoor, coordinative or strength trainings, etc.).

Interestingly, in our study the effects on physiological parameters such as maximal performance in wattage and VO_2 peak/kg in spiroergometry, could only be demonstrated for the cycling condition. For the WBV condition, we could not replicate a correlation between cardiovascular fitness and improvement of depression, stated in previous studies

for endurance training [8, 39]. So both conditions seem to attain anti-depressive effects via differing causal agents. Same could be seen for the performance in mechanography (jump performance in wattage/kg) and the anthropometric data (BMI, calipometry). Those findings suggest that the anti-depressive effects of whole body vibration treatment have to work via different mechanisms, compared to endurance sports. It will be important to investigate those mechanisms based on the existing data from adult studies, e.g., if WBV influences inflammation or growth factors in blood or liquor or leads via neurogenesis to the anti-depressive effects. Further analysis is needed to address those issues.

Strengths and limitations of the study

To our knowledge, the study “Mood Vibes” was the first program implementing a high-frequency anti-depressive exercise therapy to clinically diagnosed medication-naïve adolescents in an inpatient ward. In addition to that, it was a novelty to investigate if passive whole body vibration (WBV) exercise has comparable anti-depressive effects to an endurance cycling condition. In contrast to other interventional studies, our program administered structured and supervised exercise with comparable intensity for every subject, calculated on the personal performances in a prior spiroergometry. Our study tried not only to address the clinical outcome (i.e., depression scores), but investigated also psychological and physiological (cardiovascular) effects. With regard to the physiological parameters, an additional monitoring of lactate levels, heart rate and energy expenditure in the trainings would have presented an advantage. As a strength, we consider that most factors inherent to TAU treatment itself (i.e., the additional therapies and treatments of each patient) were assessed.

Obviously, the most important limitations are the lack of a blinded clinician rating such as the CDRS-R and the absence of randomization for the control condition. Because individuals were taken into the control group who wanted to participate in the measurements but not in the interventions, there are several sources of bias possible. A lower motivation of the not randomized control group could have influenced the results. Moreover, the results could be influenced by the exclusion of participants who performed less than two assessments or did not attend sufficiently the training sessions. Thus, the relatively high level of dropouts can have to be mentioned as an additional limitation of the study. On the other hand, considering the psychological and motivational confounders, a placebo-sports condition would be more conclusive than TAU and should also be implemented in a future study. As an additional limitation, we have to see that the underlying mechanisms of action in the neurobiological sense were not analyzed for the different intervention groups. Here, future research will be crucial. The standard

deviation of FBB–DES was relatively large which could have been caused by the fluctuation of staff in the inpatient setting and might have reduced the validity of the measure. And even if the effects in the intervention groups were high and the sample size already adequate, the findings should be repeated on a bigger sample for validation.

Conclusion

To conclude, in our study “Mood Vibes” we found strong support for the effectiveness of whole body vibration training as add-on exercise treatment in depressed adolescents. This novel finding could have important clinical implications as it can be applied in highly depressed adolescents, without drive to exercise, before more active physical activities can be administered. Furthermore, both exercise interventions (cycling condition as well as WBV) were found to be superior to TAU. Exercise interventions showed quicker and after week 26 significantly greater reduction in depression scores compared to TAU. Remission rates (calculated on DIKJ scores < 18 for the two intervention groups together) amounted to 39.7% after week 6, 48.6% after week 14 and 66% after week 26, compared to 25% after week 26 in TAU. So exercise interventions of 30 min 4 times/week seem to be sufficient for anti-depressive effects. Improvement in cardiovascular fitness did not influence the anti-depressive effects. Also motivational and psychological factors were not found to be confounders. Therefore, other neurobiological factors could play the main role. In further research the underlying mechanisms of action should be in the focus. A subsequent trial with randomized placebo-sports condition and blinded clinician rating on a larger sample would be desirable to confirm our findings.

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Compliance with ethical standards

Ethical standards The study has been approved by the appropriate ethics committee and was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Conflict of interest The authors declare that they have no conflict of interest.

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