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## A systematic review of trials investigating strength training in schizophrenia spectrum disorders

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#### ABSTRACT

This systematic review analyzed strength training (ST) in patients with schizophrenia. Two independent reviewers searched PubMed and CENTRAL. Only two studies reported on the effects of isolated ST. ST with a single exercise did not improve psychopathology but walking performance. ST for several large muscle groups significantly improved muscle strength and psychopathology. To date, no treatment recommendations can be made for ST. Consistent with recommendations for healthy people combined strength and endurance training can be recommended for schizophrenia. For higher transparency regarding trainings aspects, we recommend for future studies to use the sport science checklist proposed in this paper.

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Muscle strength is inversely associated with long-term mortality risk (Rantanen et al., 2000) and the incidence of metabolic syndrome in initially healthy men (Jurca et al., 2005). These effects appear contrary to the increased risk of cardiometabolic complications in schizophrenia (de Hert et al., 2011; Srihari et al., 2013). The benefits of strength training (ST) on psychopathology have not been investigated in sufficient detail, but some results indicate improvements of mood and anxiety (Cassilhas et al., 2010; Stanton et al., 2013) and thus positive effects on symptom severity in psychiatric disorders are to be expected.

The aim of this systematic review was to differentiate between the effects of ST and those of other types of training in schizophrenia patients. This report will serve as an addition to the published reviews on aerobic exercise and exercise in general and bridge the evidence gap regarding ST (Chalfoun et al., 2016; Dauwan et al., 2015; Firth et al., 2015; Gorczynski and Faulkner, 2010; Stanton and Happell, 2014; Vancampfort et al., 2015b; Vancampfort et al., 2015a). To design effective add-on sports programs it is essential to know and understand the effects and mechanisms of each component, i.e., strength or endurance training.

This systematic review was performed in accordance with the PRISMA recommendations (Liberati et al., 2009; Moher et al., 2009).

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Methods were specified in advance in a protocol including eligibility criteria, definitions, search terms and data items (see Supplementary material). Two reviewers (K.K.-V., P.A.V.) performed a systematic search of the PubMed database (National Center for Biotechnology Information, NCBI, National Library of Medicine, NLM) and Cochrane Central Register of Controlled Trials (CENTRAL) The search was last updated on August 09, 2016. Additionally, we extracted data on risk of bias and conducted quality ratings for the analyzed trials with the Downs and Black Quality Index (Downs and Black, 1998). To investigate trials that had been registered but had not yet published we searched "clinicaltrials.gov" and the "WHO International Clinical Trials Registry Platform Search Portal".

The search identified 320 records (see Fig. 1, Supplementary material). Additional information on the excluded studies (Archie et al., 2003; Bredin et al., 2013; Fogarty et al., 2004; Nuechterlein et al., 2014; Pelham et al., 1993; Smith and Figetakis, 1970; Strassnig et al., 2015; Takeda et al., 2002) is also presented in the Supplementary material. Four of the nine finally selected reports covered the same study, so that a total of six studies were available for qualitative analysis.

Table 1 shows detailed characteristics and the results of the six studies. The results of the Cochrane Collaboration's tool for the assessment of the risk of bias are shown in Table 2 in the Supplementary material.

Only two studies examined the impact of isolated ST in patients with schizophrenia (Heggelund et al., 2012; Silva et al., 2015). An 8-week

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**Table 1**Characteristics and results of individual studies

Characteristics and results of individual studies.				
Reference & design	Patients (sample)	Intervention incl. comparators	Outcomes in EG	Attendance and dropout rate
Heggelund et al. (2012) Controlled trial	n = 16, diagnosis of schizophrenia, schizotypal or delusional disorders (ICD 10: F20-F29); mean age: 38 y; mean PANSS: 61; 5 male completers, 8 female completers; in-and outpatients; department of psychiatry at a university hospital (monocentric); neuroleptics	8 weeks, 3 sessions/week Experimental group (EG): maximal strength training; n = 7; 5 min warm-up (treadmill, 70% intensity), leg press exercise ("54° incline leg press machine" (Heggelund et al., 2012, p. 3), controlled, 90° knee angle, rapid extension; 4 sets, 4 repetitions; 3 min rest between sets; 85–90% of 1RM; continuous increases; supervised) Control group (CG): computer game (Tetris); n = 9; 36 min/session; monitored	†* (+19.7%) Efficiency of walking (percentage of the work input and work output in treadmill exercise test) $\downarrow (-5.6\%) \text{ VO}_{2\text{peak}} \text{ (incremental treadmill exercise test)} \\ \uparrow (+38.1\%) \text{ 1RM (leg press test)} \\ \uparrow (+17.2\%) \text{ Symptoms of schizophrenia (PANSS)} \\ \uparrow (+13.3\%) \text{ Physical and } \downarrow (-2.8\%) \\ \text{mental health aspects of health-related quality of life (SF-36)} \\ \label{eq:percentage}$	Adherence rate: $85 \pm 9\%$ in EG, $83 \pm 6\%$ in CG $86\%$ completed EG $3$ dropouts (1 in EG, 2 in CG); reasons: $<80\%$ adherence (1), disappeared (1), discharged (1)
Silva et al. (2015) RCT	n = 47, schizophrenia (DSM-IV); mean age: 33 y, PANSS: 63; all male; stable medication (6 weeks); 2 sites: Centro de Atenção Psicossocial and Faculdade de Ciências Médicas da Santa Casa de São Paulo (multicentric)	3 familiarization sessions, 20 weeks, 2 session/week, 60 min/session, 5 min warm-up (treadmill, 4 km/h) Experimental group I (EGI): "RESEX"; n = 14; "progressive resistance training program", (exercises for large muscle groups: leg press, leg curl, vertical traction, chest press, arm extension, arm curl, abdominal crunch; Technogym equipment; 40–85% of 1RM; 2–3 sets, 6–15 repetitions; 1–2 min interval) Experimental group II (EGII): "CONCEX"; n = 17; resistance training like RESEX (reduced sets: 1–2); endurance training, treadmill, 40–75% of VO <sub>2max</sub> ); HR monitoring Control group (CG): "CTRL"; n = 16; same protocol; minimum load; 15 repetitions; 1 min rest; minimum	↓* $(-23.5\%/-15.8\%)$ Symptom severity (PANSS) ↓ $(-74.6\%/-67,1\%)$ depressive symptoms (CDSS) ↑ $(+22.4\%/+11.4\%)$ Health-related quality of life (SF-36) ↓ $(-55.4\%/-4.2\%)$ Biomarkers (analyses of BDNF) ↓ $(-1.1\%/-0.02\%)$ body mass ↑ $(+22.9\%/+10.9\%)$ 1 RM leg press ↑ $(*+26.6\%/+10.4\%)$ 1 RM chest press	Adherence rate: >75% 86% completed in EGI 13 dropouts (2 in EGI, 8 in EGII, 3 in CG); reasons: protocol violation (8), disease (1), job (2), hospitalization (2)
"TOPFIT" (Scheewe et al., 2012b; Scheewe et al., 2012a; Scheewe et al., 2012c; Svatkova et al., 2015) RCT	n = 63, diagnosis of schizophrenia spectrum disorder (DSM-IV); mean age: 30 y; mean PANSS: 63; 46 male, 17 female; antipsychotics; IQ > 70;University Medical Center Utrecht, Netherlands; regional mental health care institutes (multicentric)  MRI scans: n = 34  DTI scans: n = 33  CRF analysis: n = 33	speed (4 km/h) 6 months, 2 sessions/week, 60 min/session Experimental group (EG): n = 31; cardiovascular exercises; muscle strength exercises (6 exercises/session: biceps, triceps, abdominal, quadriceps, pectoral, and deltoid muscles, 3 sets, 10–15 repetitions; supervised; logbook; strict protocol; stepwise increase of intensity (week 1–3, 45%; week 4–12, 65%; week 13–26, 75% of HR reserve) Control group (CG): occupational therapy; n = 32; "creative and recreational activities such as painting, reading, and computer activities"	Cardio-respiratory fitness (CRF): $\uparrow^*$ (+0.9%) highest relative oxygen uptake $\uparrow^*$ (+9.7%)" peak work rate at the moment of exhaustion" (Scheewe et al., 2012b, p. 1835) $\downarrow^*$ (-10.7%) Symptom severity (PANSS) $\downarrow$ (-30.2%) depressive symptoms (MADRS) $\downarrow$ (-11%) BMI MRI data: $\downarrow$ (-0.1%) intracranial volume, $\downarrow$ (-0.2%) total cerebrum, $\downarrow$ (-0.2%) grey matter, $\downarrow$ (-0.1%) white matter, $\uparrow$ (+0.2%) lateral ventricle, $\rightarrow$ (0%) third ventricle, $\downarrow$ (-1%) hippocampal volume, brain connectivity ( $\uparrow^*$ fractional anisotropy) Glucose and lipids (blood analyses): no sign. Changes Blood pressure and heart rate: no sign. Changes $\uparrow$ (+4.9%) Intelligence	Attendance rate: 41 of 52 sessions; 72% >50% attendance! (n = 20 patients in EG and n = 19 patients in CG met minimal attendance [50%]); 93% completed exercise (attendance <50% not defined as dropout!) 9 dropouts (2 in EG, 7 in CG; significant difference); reasons: relapse (1), refuses to come (1), pregnancy (1), disinterest (3), personal reasons (1), lost contact (2)
Kim et al. (2014) Controlled trial	n = 40, paranoid schizophrenia (DSM-IV); mean age: 49 y; regular medication; hospitalized >3 y; Hyundae-Somang Psychiatry Unit, Eumseong-gun, Chungcheongbuk-do (monocentric)	12 weeks Experimental group (EG): $n=25$ ; 3 sessions/week; 60 min/session: 10 min warm-up (stretching), 25 min strength training (8 exercises: "chest press, seated row, squat, shoulder press, biceps curl, triceps extension, calf raise, reverse crunch, "(Kim et al., 2014, p. 793) elastic band [thera], RPE 12–13), 25 min walking (60% of individual $VO_{2max}$ , week 1–4: 50% of HRR, week 5–8: 60% of HR reserve, week 9–12: 70% of HR reserve); heart rate monitoring; RPE scale,	quotient Body composition: $\downarrow^*(-1.3\%) \text{ weight, } \downarrow^*(-3.8\%) \text{ waist circumference} \\ \text{Physical function and muscle strength } \downarrow^*(-18\%) \text{ YMCA step test, } \uparrow^*(+20.9\%) \text{ Jump test, } \uparrow^*(+247.5\%) \\ \text{sit-and-reach test, } \uparrow^*(+247.5\%) \\ \text{standing on one leg with eyes closed test, } \uparrow^*(+5.5\%) \text{ grip force, } \uparrow^*(+47.6\%) \\ \text{isometric quadriceps force } \uparrow^*(+21.5\%) \text{ BDNF serum levels } \downarrow^*(-7.1\%) \text{ Systolic blood pressure, } \downarrow^*(-8.4\%) \text{ Diastolic blood pressure, } \downarrow^*(-6.7\%) \text{ Resting heart rate} \\ \end{cases}$	4 dropouts (1 in EG, 3 in CG), reasons: personal reasons, health reasons not related to intervention

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