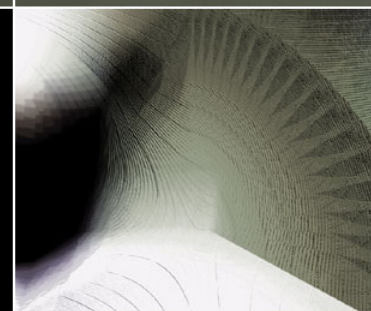


Physical activity as an adjunct treatment for schizophrenia and related psychotic disorders: A systematic review

Brad Holowachuk
Erin Hvidston
Andrea Mitchell
Rachel Richards
Melissa Richmond

Supervisor: Dr. Darlene Redenbach



Outline

- Introduction
- Methods
- Results & Discussion
- Conclusion

Introduction

- Schizophrenia:
 - severe psychiatric illness
 - median incidence 15.2 per 100, 000; male>female (McGrath et al., 2004)
 - onset adolescence (Andreasen, 1995)
 - features:
 - cognitive, sensori-perceptual, motor, and emotional disturbances; reality distortion

Psychiatric Profile of Schizophrenia

- Positive and negative symptoms (Andreasen, 1995)

Positive	Negative
delusions hallucinations thought disorganization catatonia	affective flattening loss of pleasure/interest de-motivation social withdrawal psychomotor dysfunction

- Depression and anxiety also prevalent
(Goodwin et al., 2003; Siris et al., 2001)
- Variability in clinical presentation (Andreasen, 1995)
- Decline in psychosocial, behavioural, and occupational functioning

Treatment of Schizophrenia

- primarily anti-psychotic medication

(Brenner et al., 1992)

- side-effects:

- sedation
- weight-gain/obesity
- metabolic and cardiovascular disorders
- motor disturbances

(Freedman, 2003; Schultz et al., 2007)

- 5 - 25% respond poorly requiring alternate therapies

(Brenner et al., 1992; Patterson and Leeuwenkamp, 2008)

Complications of Treatment

1) Comorbidity

- Medication and lifestyle factors

2) Psychiatric Relapse

- poor therapeutic response (Brenner et al., 1992)
- factors influencing non-adherence (Robinson et al., 2002; Stanniland and Taylor, 2000; Valenstein et al., 2004)
- substance abuse (Addington and Addington, 1997; Cantor-Graae et al., 2001; Hambrecht and Hafner, 1996; Schultz et al., 2007)
- stress (Gispén-de Wied, 2000; Schultz et al., 2007)

Social and Economic Sequelae

- Comorbidity and relapses experienced by patients lead to:

↓ patient participation in society

↑ economical and social costs for families and the health care system

(Lauber et al., 2005; Wong and Van Tol, 2003)

- **Need to identify adjunct treatments to mitigate such complications**

Exercise as Adjunct Treatment

- reduces stress levels in healthy adults
(Wijndaele et al., 2007)
- helps reduce symptoms of clinical depression
(Babyak et al., 2000; Lawlor and Hopker, 2001)
 - effect equivalent to cognitive therapy
 - decreases relapse rates
- helps reduce symptoms of clinical anxiety
(Petruzzello et al., 1991)
- reduces medical comorbidity in persons with schizophrenia
(Skinar et al., 2005; Faulkner et al., 2003)

Exercise as Adjunct Treatment

- Insufficient evidence concerning the effects of exercise on psychiatric and psychological outcomes in schizophrenia

Exercise as Adjunct Treatment

- Systematic reviews on this topic:
 - Contain only physiological outcomes (Faulkner et al., 2003)
 - Contain few and methodologically weak studies (Bradshaw et al., 2005)
 - Embed exercise within a broader category of treatments (Crawford-Walker et al., 2005)
 - Current protocol includes only RCTs (Campbell and Foxcroft, 2003); a significant limitation since majority of research is quasi-experimental (Faulkner & Biddle, 1999)

Overall Impression

- Need to determine whether exercise can influence psychiatric and psychological outcomes in schizophrenia as demonstrated for other clinical populations

(Babyak et al., 2000; Lawlor and Hopker, 2001; Petruzzello et al., 1991)

- Evidence to support exercise as an adjunct treatment may produce:
 - more comprehensive therapy
 - better adherence → reducing relapse
 - ↑ therapeutic effectiveness

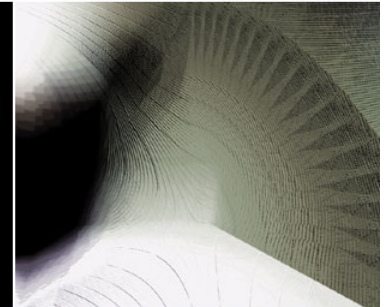
Systematic Review Statement

- To systematically assess the effects of physical activity on psychological and psychiatric outcomes in persons with schizophrenia and related psychotic disorders

Definitions and Format

- Physical activity is inclusive of exercise, and is defined as, “bodily movement that is produced by the contraction of skeletal muscle and that substantially increases energy expenditure” (Whaley, 2006)
- This review was conducted in accordance with the National Health Service Centre for Reviews and Dissemination (2001) CRD Report 4.

Methods



Methods

- Eligibility Criteria
- Search Strategy
- Study Selection
- Quality Assessment
- Data Extraction
- Data Synthesis

Eligibility Criteria

- **Subject Characteristics**
 - Persons with schizophrenia or related psychotic disorders (schizoaffective, schizophreniform, and bipolar disorder with psychotic features)
 - Subjects with concurrent brain pathology, major depression and psychoses were excluded

Eligibility Criteria

- **Intervention**
 - Physical activity in isolation or concurrent with other interventions (e.g. cognitive therapy)
 - All other regular maintenance treatment included (e.g. medications)

Eligibility Criteria

- **Outcomes**
 - Psychiatric and psychological outcome measures
 - Studies reporting only physical/physiological outcomes were excluded
 - Outcome measures with no reliability/validity were excluded

Eligibility Criteria

- **Study characteristics**
 - Peer reviewed, quantitative studies
 - 1960 to present day
 - Published and grey literature
 - French and English and foreign language abstracts with sufficient data

Search Strategy

- **Four fold strategy**
 - Electronic database search
 - Hand search
 - Reference search
 - Author contact

Study Selection

- Independently conducted by two reviewers
- Reviewers were blinded to authors' names
- Level of agreement was recorded
- Disagreements mediated by a third reviewer
- Inter-rater agreement at full text stage was 'excellent' (Landis and Koch, 1977)
 - $\kappa = 0.93$

Quality Assessment

- Two measures used to assess methodological quality
 - Bradshaw et al. (2005) adaptation
 - Jadad et al. (1996)
- Pilot tested by three reviewers on literature concerning exercise and depression
- QA of included studies conducted by two independent reviewers
- Protocol for agreement/disagreement followed as described in study selection

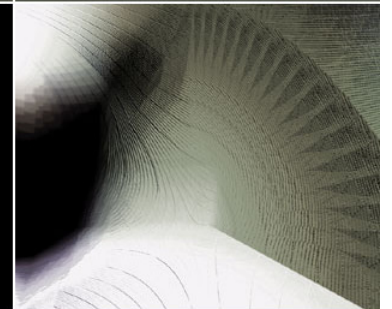
Data Extraction

- Forms created and pilot tested by two reviewers
- Data extracted independently then compared and compiled

Data Synthesis

- Descriptive synthesis planned due to expected heterogeneity of included studies

Description of Studies



Description of Studies

- Subjects
- Study Design
- Interventions
- Outcome Measures
- Other

Description of Studies

- **Description of studies**
 - 271 abstracts consistent with eligibility criteria
 - 67 full text articles
 - 59 available in French or English (5 in foreign languages, 3 unavailable in print)
 - 15 met eligibility criteria for review

Description of Studies

- **Subjects**
 - 400 subjects
 - 209 males
 - 113 females
 - 78 unknown
 - Mean age of 35.7 years (2 studies did not provide age data)
 - 9 of 15 studies used standardized diagnostic criteria
 - 9 studies in USA; 1 in each of Canada, Scotland, Israel, India and Spain

Description of Studies

- **Study Design**

- 4 RCTs, 9 quasi experimental designs, 1 case series, 1 case study
- 4 completed in an inpatient hospital setting, 8 in an outpatient setting, 1 took place in the community, 1 occurred in a mixed inpatient/outpatient setting
- Duration of studies ranged from 4 weeks to 10 years with follow up phases as long as 2 years

Description of Interventions

- **RCTs (n=4)**

- Treadmill walking vs. non-exercise (Beebe et al., 2005)
- Physical exercise vs. relaxation (Canarvis, 1996)
- Yoga therapy vs. physical exercise therapy (Duraismamy et al., 2007)
- Holistic treatment vs. social skills treatment (Lukoff et al., 2007)

Description of Interventions

- **Quasi experimental studies (n=9)**
 - Walking vs. treatment as usual (Ball et al., 2001)
 - Recreational games and skills (Bergman et al., 1993)
 - Fitness training (Centorrino et al., 2006)
 - Aerobic exercise (Fuller, 1990; Jorgensen, 1986)
 - Outdoor adventure vs. treatment as usual (Kelley et al., 1997)
 - Running vs. waiting to run, random activities, meditation, new meditation (Levin, 1983)
 - Active vs. passive therapeutic recreation (Morris et al., 1999)
 - Exercise vs. standard care (Torres-Carbajo et al., 2005)

Description of Interventions

- **Case series (n=1)**
 - Aerobic exercise on a stationary bike
(Pelham and Campagna, 1991)
- **Case study (n=1)**
 - Weight training (Adams, 1995)

Description of Studies

- **Outcome Measures**
 - 36 outcome measures identified
 - Psychiatric (anxiety, depression, clinical severity, psychomotor symptoms, relapse rate)
 - Psychological (behavioural scales, self concept, self efficacy, self image, quality of life, and functioning)
 - Outcome measures divided into 12 categories based on criteria assessed

Description of Studies

- **Other**
 - Attrition
 - Adverse events
 - Health screen
 - Compensation

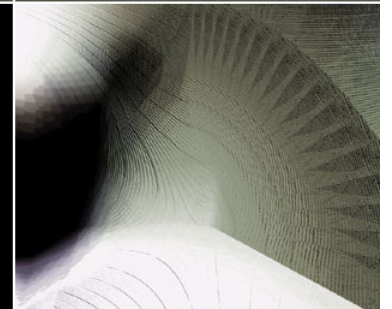
Results

- **Methodological Quality**
 - Bradshaw et al. (2005):
 - mean = 56% (range of 35-82%)
 - n=4 < 50%, n=9 50-75%, n=2 > 75%
 - Items with low scores presented in discussion
 - 'substantial' agreement ($\kappa=0.71$) (Landis and Koch, 1977)
 - Jadad et al. (1996):
 - mean= 0.80 (range of 0 - 2)
 - lack of double blinding and random assignment
 - attrition underreported
 - 'substantial' agreement ($\kappa =0.73$) (Landis and Koch, 1977)

Grading of Evidence

- Cochrane Musculoskeletal Group (2006) method of grading
 - Silver
 - Small sample sizes
 - Limited blinding of assessors
 - No blinding of subjects to intervention

Results & Discussion



Results & Discussion Outline

- **1 – Results & Discussion of Outcomes**
- **2 – Limitations**
- **3 – Recommendations**

Results of Outcomes

- **Anxiety and Depression**
- Behaviour
- **Global Psychiatric Symptom Severity**
- Locus of Control
- Pain
- Psychomotor
- **Quality of Life and Functioning**
- **Relapse Rate**
- Self Concept and Self Efficacy
- Self Image
- **Symptoms of Schizophrenia**
- Trust and Cooperation

Outcome: Anxiety & Depression

- 7 studies
- RCTs - Anxiety
 - Holistic health vs. social skills training found no significant differences between groups (Lukoff et al., 1986)
 - Physical activity vs. relaxation found no between group differences but significant within group reductions (Canarvis, 1996)

Outcome: Anxiety & Depression

- Quasi Experimental
 - adventure group had significant decreases in anxiety and depression compared with controls (Kelley et al., 1997)
 - aerobic exercise group had significant decreases in anxiety and depression compared with controls (Levin, 1983)
 - 2 additional studies using aerobic interventions reported improvements, but not significant between-group differences (Jorgensen, 1986; Ball et al., 2001)

Outcome: Anxiety & Depression

- Case series
 - general trend of a reduction in depression (Pelham and Campagana, 1991)

Outcome: Anxiety & Depression

- **Most studies demonstrated decreases in symptoms**
- **Underlying cause may be due to co-existing condition and not symptoms of schizophrenia**
- **Future research should consider focusing on symptoms specific to schizophrenia**

Outcomes: Global Symptom Severity

- 8 studies
- RCTs
 - no between, but significant within-group improvements in overall psychiatric status for both holistic and social skills groups (Lukoff et al., 1986)

Outcomes: Global Symptom Severity

- Quasi experimental studies
 - significant between-group difference showing decreases in Somatization and Hostility for aerobic exercise condition (Jorgensen, 1986)
 - significant between-group difference with reduced Interpersonal sensitivity and Hostility in outdoor adventure condition (Kelley et al., 1997)
 - no significant between-group differences; significant within-group reductions in Obsession/Compulsion, and Phobic Anxiety for aerobic exercise condition (Levin, 1983)
 - no significant differences (Ball et al., 2001; Bergman et al., 1993; Centorrino et al., 2006)

Outcomes: Global Symptom Severity

- Case Series
 - general trend of increasing improvements over time with structured exercise (Pelham and Campagna, 1991)

Outcomes: Global Symptom Severity

- Few significant between-group differences
- Significant change within groups
- Results may indicate clinical significance

Outcomes: Relapse Rate

- 2 studies
- 1 RCT found no significant differences between holistic health and social skills intervention (Lukoff et al., 1986)
- 1 quasi experimental study found significantly fewer relapses for the exercise group compared to the control group (Torres-Carbajo et al., 2005)

Outcomes: Relapse Rate

- **Not often examined**
- **Economic / social impact on family and health care system indicates this measure should be addressed in future studies**

Outcomes: Quality of Life & Functioning

- 2 studies
- Yoga therapy (YT) had significant improvement in QOL and functioning compared with physical training (PT) (Duraismamy et al., 2007)
- Within-group differences were found for functional measures in both YT and PT
- 1 study found no effect of exercise on QOL (Centorrino et al., 2006)

Outcomes: Quality of Life & Functioning

- **Yoga shown to increase QOL and functioning**
- **Due to self-reflective nature of yoga?**

Outcomes: Symptoms of Schizophrenia

- 7 studies
 - 1 RCT found significant reduction in symptoms for yoga group as compared with physical training; and significant within-group reductions for both (Duraiswamy et al., 2007)
 - 1 RCT demonstrated significant within-group reductions for both holistic health and social skills groups (Lukoff et al., 1986)
 - 1 RCT found clinical significance (Beebe et al., 2005)
 - 3 quasi experimental studies showed no change (Ball et al., 2001; Centorrino et al., 2006; Fuller, 1990), and 1 case study found an increase in symptoms (Adams, 1995)

Outcomes: Symptoms of Schizophrenia

- **Between-group and within-group significance**
- **Results may indicate clinical significance**
- **Subtype analyses concerning diagnosis may allow increased sensitivity of findings**

Outcomes: Other

- **Outcomes not as readily addressed:**
 - Self-efficacy / concept
 - Self-image
 - Locus of control
 - Pain
 - Psychomotor
 - Behavioural
 - Trust and co-operation
- **Should be considered as future studies emphasize a more holistic treatment approach**

Results & Discussion Outline

- 1 – Results & Discussion of Outcomes
- **2 – Limitations**
- 3 – Recommendations

Limitations: Breadth of Literature

- **Main focus is on physiological outcomes**
 - Cardiovascular fitness
 - Weight loss
- **Literature on psychological outcomes is generally lacking**

Limitations: Heterogeneity

- **Study design**
 - Ranged from RCTs to case study
 - Majority quasi-experimental
- **Population characteristics**
 - Research setting, diagnosis, sample size, medications
- **Intervention**
 - Standardization: design and supervision
 - Follow up

Limitations: Methodological Quality

- Generally poor
- Highlighted in “Recommendations” section

Limitations: Summary

- **Further limitations imposed by inclusion criteria**
- **Limitations compounded to create bias**
- **Attempts to mitigate bias:**
 - Standardized guideline for review
 - Inclusion of various forms of literature

Discussion Outline

- 1 – Results & Discussion of Outcomes
- 2 – Limitations
- **3 – Recommendations**
 - Diagnostic Criteria
 - Sample Size
 - Physical Activity Criteria
 - Follow Up
 - Other

Methodological Issue: Diagnostic Criteria

- **Methodological Issues:**
 - Standardized diagnostic criteria not used / reported by many studies
 - Subtypes often not classified
 - Lack of criteria weakens credibility of the study

Recommendations: Diagnostic Criteria

- **Recommendations:**
 - Utilize standardized diagnostic criteria (e.g. DSM)
 - Include subtype diagnoses to account for various presentations

**Strengthens causal relationship
between physical activity and
symptoms of schizophrenia**

Methodological Issue: Sample Size

Methodological Issues:

- Consistently small sample sizes
- No power calculations

Recommendations:

- Perform power calculations when appropriate
- Increase sample size when possible

Improves ability to detect change

Methodological Issue: Physical Activity Criteria

Methodological Issue:

- Few studies included interventions designed and supervised by qualified personnel

Recommendations:

- Follow standardized criteria (e.g. ACSM) and ensure supervision

Allows for comparison between physical activity interventions and increases the credibility of the results

Methodological Issue: Follow Up

Methodological Issue:

- Few studies demonstrated appropriate follow up

Recommendation:

Perform follow up within a time frame in which physical activity effects are maintained

Methodological Issue: Other

- **Subject selection**
 - Randomization vs. convenience sampling
- **Baseline comparison**
 - Undetected between subject variability
- **Medication standardization**
 - Chlorpromazine equivalents as covariate
- **Attrition**
 - Underreported and misreported
- **Adverse effects / events**
 - Underreported

Summary of Recommendations

- Standardized diagnostic criteria
- Adequate sample size
- Standardized physical activity interventions
- Design / supervision for physical activity interventions
- Subtype analyses by diagnostic category
- Appropriate follow up
- Consider sampling methods, baseline data collection, medication standardization, attrition reporting and adverse events.

Conclusion

- Results not sufficient to indicate that physical activity can produce a significant change in outcomes
- There is, however, suggested clinical relevance for many of the findings

Conclusion

- Given that physical activity is beneficial to overall health and mental well being, it may be considered a useful adjunct treatment.
- Using improved methodological standards, future research may result in a higher level of evidence and thus may more clearly demonstrate the role of physical activity as an adjunct to psychological and psychiatric treatment.
- This review provides a compendium upon which future research can be based.

Acknowledgements

Special thanks to:

- Dr. Darlene Redenbach
- Dr. Angela Busch
- Charlotte Beck
- Melissa Canarvis, Kathi Fuller, Dr. Cathy Jorgensen, and Dr. Stephen Levin
- Physiotherapist Inge Kreuzer and recreational therapist Donna Beniusis of Riverview Hospital in Coquitlam B.C.

References

- Adams, L., 1995. How exercise can help people with mental health problems. *Nursing Times*. 91 (36) 37-39.
- Addington, J., Addington, D., 1997. Substance abuse and cognitive functioning in schizophrenia. *J Psychiatry Neurosci*. 22 (2) 99-104.
- Andreasen, N.C., 1995. Symptoms, signs, and diagnosis of schizophrenia. *Lancet*. 346 (8973) 477-81.
- Babyak, M., Blumenthal, J.A., Herman, S., Khatri, P., Doraiswamy, M., Moore, K., Craighead, E., Baldewicz, T.T., Krishnan, K.R., 2000. Exercise treatment for major depression: Maintenance of therapeutic benefit at 10 months. *Psychosomatic Medicine*. 62 633-638.
- Ball, M. P., Coons, V. B., Buchanan, R. W., 2001. A program for treating olanzapine-related weight gain. *Psychiatric Services*. 52 (7) 967-969.
- Beebe, L. H., Tian, L., Morris, N., Goodwin, A., Allen, S. S., Kuldau, J., 2005. Effects of exercise on mental and physical health parameters of persons with schizophrenia. *Issues in Mental Health Nursing*. 26 (6) 661-676.
- Bergman, U., Hutzler, Y., Stein, D., Avidan, G., Wozner, Y., 1993. Therapeutic physical activity for adolescents in a closed psychiatric ward. *Issues in Special Education & Rehabilitation*. 8 (2) 41-54.
- Bradshaw, T., Lovell, K., Harris, N., 2005. Healthy living interventions and schizophrenia: a systematic review. *Journal of Advanced Nursing*. 49 (6) 634-654.
- Brenner, H.D., Hodel, B., Roder, V., Corrigan, P., 1992. Treatment of cognitive dysfunctions and behavioural deficits in schizophrenia: integrated psychological therapy. *Schizophr Bull*. 18 (1) 21-6.
- Campbell, P., Foxcroft, D., 2003. Exercise therapy for schizophrenia (Protocol). *Cochrane Database of Systematic Reviews*. Issue 4 Art. No.: CD004412. DOI: 10.1002/14651858.CD004412.
- Canarvis, M., 1996. Effectiveness of relaxation as compared to physical exercise in anxiety reduction for individuals with chronic schizophrenia. M.S., D'Youville College.
- Cantor-Graae, E., Nordstrom, L.E., McNeil, T.F., 2001. Substance abuse in schizophrenia: a review of the literature and a study of correlates in Sweden. *Schizophr. Res*. 48 (1) 69-82.
- Centorrino, F., Wurtman, J. J., Duca, K. A., Fellman, V. H., Fogarty, K. V., Berry, J. M., Guay, D.M., Romeling, M., Kidwell, J., Cincotta, S.L., Baldessarini, R. J., 2006. Weight loss in overweight patients maintained on atypical antipsychotic agents. *International journal of obesity*. 30 (6) 1011-1016.
- Cochrane Musculoskeletal Group, 2006. Developing a systematic review [Online]. Available from <http://www.cochranemsk.org/review/writing/>
- Crawford-Walker, C.J., King, A., Chan, S., 2005. Distraction techniques for schizophrenia. *Cochrane Database of Systematic Reviews*. Issue 1. Art. No.:CD004717. DOI: 10.1002/14651858.CD004717.pub2.
- Duraiswamy, G., Thirthalli, J., Nagendra, H. R., Gangadhar, B. N., 2007. Yoga therapy as an add-on treatment in the management of patients with schizophrenia - A randomized controlled trial. *Acta Psychiatrica Scandinavica*. 116 (3) 226-232.
- Faulkner, G., Biddle, S., 1999. Exercise as an adjunct treatment for schizophrenia: A review of the literature. *J of Mental Health*. 8 (5) 441-457.

References

- Faulkner, G., Soundy, A.A., Lloyd, K., 2003. Schizophrenia and weight management: a systematic review of interventions to control weight. *Acta Psychiatr Scand.* 108 324-332.
- Freedman, R., 2003. Schizophrenia. *New England Journal of Medicine.* 349 (18) 1738-49.
- Fuller, K., 1990. Antecedent aerobic exercise training with schizophrenic outpatients. Masters dissertation, Western Michigan University.
- Gispén-de Wied, C.C., 2000. Stress in schizophrenia: an integrative view. *European Journal of Pharmacology.* 405 (1) 375-384.
- Goodwin, R.D., Amador, X.F., Malaspina, D., Yale, S.A., Goetz, R.R., Gorman, J.M., 2003. Anxiety and substance use comorbidity among inpatients with schizophrenia. *Schizophr. Res.* 61 89-95.
- Hambrecht, H., Hafner, H., 1996. Substance abuse and the onset of schizophrenia. *Biology of Psychiatry.* 40 (11) 1155-1163.
- Jadad, A.R., Moore, R.A., Carroll, D., Jenkinson, C., Reynolds, D.J.M., Gavaghan, D.J., McQuay, H.J., 1996. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled Clinical Trials.* 17 1-12.
- Jorgensen, C., 1986. Aerobic conditioning in the therapeutic treatment of chronic schizophrenia. *Educational D.*, Northern Arizona University.
- Kelley, M. P., Coursey, R. D., Selby, P. M. (1997). Therapeutic adventures outdoors: A demonstration of benefits for people with mental illness. *Psychiatric Rehabilitation Journal.* 20 (4) 61-73.
- Landis, J.R., & Koch, G.G., 1977. The measurement of observer agreement for categorical data. *Biometric.* 33 159.
- Lawlor, D.A., Hopker, S.W., 2001. The effectiveness of exercise as an intervention in the management of depression: Systematic review and meta-regression analysis of randomised controlled trials. *BMJ.* 322 763-767.
- Lauber, C., Keller, C., Eichenberger, A., Rossler, W., 2005. Family burden during exacerbation of schizophrenia: Quantification and determinants of additional costs. *International Journal of Social Psychiatry.* 51 (3) 259-264.
- Levin, S., 1983. The effects of a ten-week jogging program as an adjunctive treatment for patients in a social rehabilitation clinic. US: ProQuest Information & Learning.
- Lukoff, D., Wallace, C. J., Liberman, R. P., Burke, K., 1986. A holistic program for chronic schizophrenic patients. *Schizophrenia bulletin,* 12 (2) 274-282.
- McGrath, J., Saha, S., Welham, J., Saadi, O.E., MacCauley, C., Chant, D., 2004. A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. *BMC Med.* 2 13.
- Morris, D., Card, J., Menditto, A., 1999. Active and passive therapeutic recreation activities: A comparison of appropriate behaviors of individual with schizophrenia. *Therapeutic Recreation Journal,* 33 (4) 275-286.
- Patterson, T.L., Leeuwenkamp, O.R., 2008. Adjunctive psychosocial therapies for the treatment of schizophrenia. *Schizophr. Res.* 100 108-119.

References

- Pelham, T. W., Campagna, P. D., 1991. Benefits of exercise in psychiatric rehabilitation of persons with schizophrenia. *Canadian Journal of Rehabilitation*. 4 (3) 159-168.
- Petruzzello, S.J., Landers, D.M., Hartfield, B.D., Kubitz, K.A., Salazar, W., 1991. A meta-analysis on the anxiety-reducing effects of acute and chronic exercise. *Sports Medicine*. 11 143-182.
- Robinson, D.G., Woerner, M.G., Alvir, J.M.J., Bilder, R.M., Hinrichsen, G.A., Lieberman, J.A., 2002. Predictors of medication discontinuation by patients with first-episode schizophrenia and schizoaffective disorder. *Schizophr. Res.* 57 209-219.
- Schultz, S.H., North, S.W., Shields, C.G., 2007. Schizophrenia: a review. *American Family Physician*. 5 (12) 1821-1830.
- Siris, S.G., Addington, D., Azorin, J.M., Falloon, I.R., Gerlach, J., Hirsch, S.R., 2001. Depression in schizophrenia: recognition and management in the USA. *Schizophr. Res.* 47 (2-3) 185-197.
- Skinar, G.S., Huxley, N.A., Hutchinson, D.S., Menniger, E., Glew, P., 2005. The role of a fitness intervention on people with serious psychiatric disabilities. *Psychiatric Rehabilitation Journal*. 29 (2) 122-127.
- Stanniland, C., Taylor, D., 2000. Tolerability of atypical antipsychotics. *Drug Safety*. 22 195-214.
- Torres-Carbajo, A., Olivares, J. M., Merino, H., Vázquez, H., Díaz, A., Cruz, E., 2005. Efficacy and effectiveness of an exercise program as community support for schizophrenic patients. *American Journal of Recreation Therapy*. 4 (3) 41-47.
- Valenstein, M., Blow, F.C., Copeland, L.A., McCarthy, J.F., Zeber, J.E., Omon, L., Bingham, R., Stavenger, T., 2004. Poor antipsychotic adherence among patients with schizophrenia: medications and patient factors. *Schizophr. Bull.* 30 (2) 255-264.
- Whaley, M.H., editor, 2006. *American college of sports medicine guidelines for exercise testing and prescription*, seventh ed. Lippincott Williams & Wilkins, Philadelphia.
- Wijndaele, K., Matton, L., Duvigneaud, N., Lefevre, J., De Bourdeaudhuij, I., Duquet, W., Thomis, M., Philippaerts, R.M., 2007. Association between leisure time physical activity and stress, social support and coping: A cluster-analytic approach. *Psychology of Sport and Exercise*. 8 (4) 425-440.
- Wong, A.H.C., Van Tol, H.H.M., 2003. Schizophrenia, from phenomenology to neurobiology. *Neuroscience and Biobehavioural Reviews*. 27 (3) 269-306.

THANK YOU!

