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)

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>delusions</td>
<td>affective flattening</td>
</tr>
<tr>
<td>hallucinations</td>
<td>loss of pleasure/interest</td>
</tr>
<tr>
<td>thought disorganization</td>
<td>de-motivation</td>
</tr>
<tr>
<td>catatonia</td>
<td>social withdrawal</td>
</tr>
<tr>
<td></td>
<td>psychomotor dysfunction</td>
</tr>
</tbody>
</table>

- 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  (Gispen-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 \( \rightarrow \) reducing relapse
  - \( \uparrow \) 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 (Duraiswamy 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 (κ=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 (κ =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 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) (Duraiswamy 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


Canarvis, M., 1996. Effectiveness of relaxation as compared to physical exercise in anxiety reduction for individuals with chronic schizophrenia. M.S., D’Youville College.


References


References


THANK YOU!