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A Long Time Coming – The Creation of an Evidence Base for Physical Activity Prescription to Improve Health Outcomes in Bipolar Disorder

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While there have been several reviews published on the beneficial effects of physical activity and mood disorders (e.g., Daley, 2008), clinical research into the role of physical activity as an adjunctive treatment for persons with serious mental disorders, notably bipolar disorder, has been less common. This void probably reflects the historical fact that most research on the relationship between physical activity and mental health was conducted in exercise science labs, which may have precluded those with serious mental illness such as bipolar disorder from participating. Research on patients with serious mental illness was approached cautiously due to ethical concerns about aggravating patient symptoms or possessing adequate clinical training to manage potential psychiatric adverse events.

Despite increased recognition over the past decade that bipolar disorder imposes a tremendous health burden on society due in part to the substantial risk for cardiovascular disease among persons with this condition (Fagiolini, Chengappa, Soreca, & Chang, 2008; Kupfer, 2005), behavioral health interventions designed to address these physical health disparities have lagged. The absence of basic or applied physical activity research studies for serious mental illnesses such as bipolar disorder is even more surprising given that physical activity is frequently recommended as an essential treatment for improving patient outcomes (American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, & North American Association for the Study of Obesity, 2004; De Hert, et al., 2009; Fagiolini & Goracci, 2009) including in multi-component clinical trials (e.g., Kilbourne, Post, Nossek, Drill, et al., 2008). Moreover, bipolar disorder engenders unique characteristics that make physical activity interventions important for this group. Notably, persons with this illness experience a wide range of functioning and alternating periods of depression and mania, the former leading to sedentary lifestyle and the latter leading to excessive behaviors such as overeating that can lead to weight gain.

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Articles appearing in *Mental Health and Physical Activity* reflect a turning point in the literature whereby a nascent evidence base has been started to provide clinicians with information specifically tailored to issues affecting the prescription of physical activity for patients with bipolar disorder. Kim Wright and colleagues (Wright, Everson-Hock, & Taylor, 2009) present the first systematic review of the effects of physical activity on physical *and* mental health outcomes. Despite the dearth of clinical trials examining the effect of physical activity on relevant outcomes relating to bipolar disorder (e.g., neuro-cognitive pathways, mood management, or health outcomes), the review's survey of the medical and psychiatric literature highlights numerous opportunities for high impact research and intervention. Notably, the authors outline a roadmap of key basic science and translational research topics that will further advance the application of physical activity for the treatment of bipolar disorder.

The cross-sectional report by John Cairney and colleagues (Cairney, Veldhuizen, Faulkner, Happitots, & Rodriguez, 2009) also marks the first national epidemiological study to specifically examine correlates of physical activity behavior in patients with bipolar disorder. While prior cross-sectional survey studies have been published on self-reported physical activity habits of persons with bipolar disorder, none have exclusively examined physical activity behavior with such a large sample. The authors acknowledge sampling issues and self-report biases may have contributed to the nonsignificant differences in physical activity levels reported by the respondents with bipolar disorder, major depression, or no mood disorder. However, they also recognize that future studies employing objective methods to assess physical activity patterns for discrepancies between perceived and actual physical activity levels may reveal subtle differences in physical activity patterns that may contribute to the high rates of obesity and metabolic syndrome among bipolar patients (Janney, et al., 2008; Troiano, et al., 2008). Together, these seminal studies exemplify the aims of this journal to grow the evidence base for application of physical activity into mental health treatments by providing a supportive forum for high quality research studies (Taylor & Faulkner, 2008).

There is an urgent public health need for applied physical activity research that can be translated into interventions that improve the quality of care and health outcomes for individuals with bipolar disorder. Bipolar disorder is considered the sixth most disabling medical condition according to the World Health Organization (Murray & Lopez, 1997). Moreover, patients with bipolar disorder incur the most health care costs of any mental illness (Peele, Xu, & Kupfer, 2003; Simon & Unutzer, 1999) with many of these costs driven by co-morbid health conditions such as cardiovascular disease, diabetes, and obesity. Cardiovascular disease (CVD) is the leading cause of premature mortality for patients with bipolar disorder (Roshanaei-Moghaddam & Katon, 2009) with physical inactivity independently predicting mortality (Kilbourne, et al., 2009). In a recent study, the mean age of CVD diagnosis was 6 years younger in persons with bipolar I disorder than persons with major depressive disorder and 15 years younger than controls not diagnosed with either mood disorder (Goldstein, Fagiolini, Houck, & Kupfer, 2009). As Wright et al. and Cairney et al. both observe, these physical health risks appear to be driven by a combination of factors including unhealthy lifestyle behaviors exacerbated by mood symptoms (Kilbourne, et al., 2007), pharmacological treatment (Newcomer & Hennekens, 2007), and the allostatic load imposed by recurrent mood episodes (Kapczinski, et al., 2008), most notably the severity of manic/hypomanic episodes (Fiedorowicz, et al., 2009; D. P. Murray, Weiner, Prabhakar, & Fiedorowicz, 2009).

Bipolar disorders are inherently difficult to study and treat due to the complexity and variability of symptoms experienced by patients over time. In contrast to other serious mental illnesses, bipolar disorder is uniquely characterized by alternating periods of manic,

depressive, mixed, or euthymic episodes, leading to variations in psychosocial functioning over time (Huxley & Baldessarini, 2007). Hence, the illness is best characterized as a complex, chronic condition that must be managed, not unlike diabetes or asthma (Kilbourne, Post, Nossek, Sonel, et al., 2008). By necessity, treatment must be personalized to address the patient's unique tolerance of pharmacological therapies as well as medical and psychiatric comorbidities. In our opinion, the systematic collaboration of medical and psychiatric care that helps support ongoing symptom monitoring and self-management is the cornerstone of helping patients live with this condition. Poor management of mood symptoms can lead to psychosis and severe functional and social impairment which can further exacerbate psychological distress. Furthermore, bipolar patients are at high risk of self-medicated mood regulation with nicotine or illicit substances, without healthy alternatives.

Pharmacotherapy is the primary treatment strategy to manage bipolar disorder. However, psychosocial interventions are also essential for promoting effective self-management of both mental and physical health symptoms which includes medication adherence, healthy lifestyle habits, and regularly interacting with health providers to ensure treatment strategies are optimized while minimizing side-effects that undermine quality of life or treatment adherence. Chronic, collaborative care interventions that promote coordinated care, symptom management, and recovery of interpersonal functioning have proven cost-effective for improving functioning, quality of life, satisfaction with care, and reduced affective symptom burden for patients with bipolar disorder (Bauer, et al., 2006; Simon, Ludman, Bauer, Unutzer, & Operskalski, 2006). More recent studies implementing this model of care have put equal emphasis on managing physical and mental health risks (Bauer, Kilbourne, Greenwald, Ludman, & McBride, 2008), particularly by emphasizing regular engagement in moderate physical activity as a strategy to both cope with mood symptoms as well as to reduce risk for common cardiovascular risk factors (Kilbourne, Post, Nossek, Sonel, et al., 2008). In essence, clinicians have promoted physical activity to improve health outcomes based on the evidence from the general medical literature while having less empirical support from the psychiatric literature.

In our work testing applied behavioral interventions to help patients manage bipolar disorder, many patients anecdotally report relying on exercise as a strategy to manage both their mood symptoms and physical health risks. Many clinicians and patients believe that exercise is an effective strategy to manage negative mood states based on either trial and error, or on conventional wisdom derived from the existing literature on exercise and mood. Depressive symptoms are the most common and debilitating symptoms experienced by bipolar patients (Calabrese, Hirschfeld, Frye, & Reed, 2004). Prior research has demonstrated that physical activity can serve as both a behavioral activation strategy (Dimidjian & Davis, 2009) to improve function as well as to improve symptom coping through yet unknown neuro-cognitive pathways. However, little is known about the effectiveness of such an approach in bipolar patients who may find even residual depressive symptoms more debilitating than patients with unipolar depression.

As the Wright et al. review underscores, no studies have been conducted to examine the effect of physical activity on mania or hypomania. Longitudinal assessments of physical activity patterns might elucidate whether regular engagement in exercise reduces the frequency of manic episodes or mitigates the duration and severity of hypomanic episodes. Moreover, nothing is known regarding the acute effect of exercise on commonly experienced episodes of mixed mood states. Mood regulation researchers have observed that tension and irritability are underlying dimensions common to all negative mood states experienced in bipolar disorder including mania, depression, and anxiety (Thayer, 1996). In many cases, individuals with the worst pre-exercise affect often experience the greatest,

acute post-exercise mood improvement (e.g., Gauvin, Rejeski, & Norris, 1996; Rejeski, Gauvin, Hobson, & Norris, 1995). Whether this finding holds true for hypomania or mixed mood episodes remains an intriguing hypothesis for examination. Exercise may also present an effective strategy to regulate excess energy and to promote normalization of circadian sleep/wake patterns helpful in stabilizing mood in therapeutic approaches such as Interpersonal and Social Rhythm Therapy (Frank, 2007).

From a translational research perspective, it is important that researchers design physical activity interventions with real world settings in mind. Currently, care for bipolar disorder is highly fragmented with little coordination of patient care between mental and general medical providers. Many patients face numerous barriers to accessing physical health care treatment due to a lack of health insurance, economic difficulty, or mood episodes that cause them to lose contact with their health care provider. These disparities in care lead to poor symptom management, high risk for physical comorbidity, and ultimately premature mortality. We have found that care management that facilitates coordination of care between mental and physical healthcare improves outcomes. For example, in the Life Goals Collaborative Care model for bipolar disorder, an allied health professional provides psycho-educational sessions based on a menu of self-management strategies (Bauer, et al., 2008) including motivational coaching on physical activity to improve patient outcomes. This model of intervention helps patients develop long-term coping skills to manage their illness and is tailored to each patient's own unique health needs and psychosocial context. From an exercise prescription standpoint, the care manager serves a vital role by communicating healthcare issues to providers that commonly occur as a result of becoming more physically active (e.g., adjustment of blood pressure or diabetes medications) and providing motivational support to support long-term adoption of a physically active lifestyle. Furthermore, the care manager also informs providers of adverse side effects from psychotropic medications so that adjustments can be made so that patients do not discontinue these critical medications. In light of the known metabolic and neurological side-effects of many psychotropic drugs such as second generation atypical antipsychotics, all clinical providers could also benefit from basic research exploring how these drugs affect exercise performance, perceptions of exertion, and other motivational determinants of exercise enjoyment and adherence.

Perhaps the social stigma associated with severe manic episodes or psychosis has presented a barrier to physical activity research in persons with bipolar disorder in the past? Still, bipolar disorders are the quintessential mind-body illness that could benefit from an evidence base showing the specific benefits of exercise on health outcomes. The review by Wright et al. provides a basic blueprint for researchers in the psychiatric and exercise science communities to launch clinical studies that could vastly improve the long-term health of individuals with bipolar patients by improving both mental health outcomes and control the risk for chronic disease risk factors such as obesity, diabetes, hypertension, and hyperlipidemia. Although James Blumenthal (Blumenthal, 2009) argues that the “jury is still out...” on the effectiveness of physical activity for improving depression outcomes, we are optimistic that the advances in physical activity-depression studies over the past decade will provide guidance on the design of innovative clinical trials for bipolar disorder.

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References

- American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, & North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care* 2004;27:596–601. [PubMed: 14747245]
- Bauer MS, McBride L, Williford WO, Glick H, Kinosian B, Altshuler L, et al. Collaborative care for bipolar disorder: Part II. Impact on clinical outcome, function, and costs. *Psychiatric Services* 2006;57:937–945. [PubMed: 16816277]
- Bauer, MS.; Kilbourne, AM.; Greenwald, DE.; Ludman, EJ.; McBride, L. *Overcoming Bipolar Disorder: A Comprehensive Workbook for Managing Your Symptoms & Achieving Your Life Goals*. New Harbinger Publications, Inc.; Oakland, CA: 2008.
- Blumenthal JA. A commentary on 'Exercise and Depression' (Mead et al., 2008): And the Verdict Is.... *Mental Health and Physical Activity* 2009;2:97–99. [PubMed: 20161362]
- Cairney J, Veldhuizen S, Faulkner G, Schaffer A, Rodriguez MC. Bipolar disorder and physical activity: results from a national survey of Canadians. *Mental Health and Physical Activity* 2009;2:65–70.
- Calabrese JR, Hirschfeld RM, Frye MA, Reed ML. Impact of depressive symptoms compared with manic symptoms in bipolar disorder: results of a U.S. community-based sample. *Journal of Clinical Psychiatry* 2004;65:1499–1504. [PubMed: 15554762]
- Daley A. Exercise and depression: a review of reviews. *Journal of Clinical Psychology in Medical Settings* 2008;15:140–147. [PubMed: 19104978]
- De Hert M, Dekker JM, Wood D, Kahl KG, Holt RI, Moller HJ. Cardiovascular disease and diabetes in people with severe mental illness position statement from the European Psychiatric Association (EPA), supported by the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ESC). *European Psychiatry* 2009;24:412–424. [PubMed: 19682863]
- Dimidjian S, Davis KJ. Newer variations of cognitive-behavioral therapy: behavioral activation and mindfulness-based cognitive therapy. *Current Psychiatry Reports* 2009;11:453–458. [PubMed: 19909667]
- Fagiolini A, Chengappa KN, Soreca I, Chang J. Bipolar disorder and the metabolic syndrome: causal factors, psychiatric outcomes and economic burden. *CNS Drugs* 2008;22:655–669. [PubMed: 18601304]
- Fagiolini A, Goracci A. The effects of undertreated chronic medical illnesses in patients with severe mental disorders. *Journal of Clinical Psychiatry* 2009;70(Suppl 3):22–29. [PubMed: 19570498]
- Fiedorowicz JG, Solomon DA, Endicott J, Leon AC, Li C, Rice JP, et al. Manic/hypomanic symptom burden and cardiovascular mortality in bipolar disorder. *Psychosomatic Medicine* 2009;71:598–606. [PubMed: 19561163]
- Frank, E. *Treating bipolar disorder: A clinician's guide to Interpersonal and Social Rhythm Therapy*. Guilford Press; New York: 2007.
- Gauvin L, Rejeski WJ, Norris JL. A naturalistic study of the impact of acute physical activity on feeling states and affect in women. *Health Psychology* 1996;15:391–397. [PubMed: 8891718]
- Goldstein BI, Fagiolini A, Houck P, Kupfer D. Cardiovascular disease and hypertension among adults with bipolar I disorder in the United States. *Bipolar Disorders* 2009;11:657–662. [PubMed: 19689508]
- Huxley N, Baldessarini RJ. Disability and its treatment in bipolar disorder patients. *Bipolar Disorders* 2007;9:183–196. [PubMed: 17391360]
- Janney CA, Richardson CR, Holleman RG, Glasheen C, Strath SJ, Conroy MB, et al. Gender, mental health service use and objectively measured physical activity: Data from the National Health and Nutrition Examination Survey (NHANES 2003–2004). *Mental Health and Physical Activity* 2008;1:9–16. [PubMed: 19946571]
- Kapczynski F, Vieta E, Andreazza AC, Frey BN, Gomes FA, Tramontina J, et al. Allostatic load in bipolar disorder: implications for pathophysiology and treatment. *Neuroscience and Biobehavioral Reviews* 2008;32:675–692. [PubMed: 18199480]

- Kilbourne AM, Morden NE, Austin K, Ilgen M, McCarthy JF, Dalack G, et al. Excess heart-disease-related mortality in a national study of patients with mental disorders: identifying modifiable risk factors. *General Hospital Psychiatry* 2009;31:555–563. [PubMed: 19892214]
- Kilbourne AM, Post EP, Nossek A, Drill L, Cooley S, Bauer MS. Improving medical and psychiatric outcomes among individuals with bipolar disorder: a randomized controlled trial. *Psychiatric Services* 2008;59:760–768. [PubMed: 18586993]
- Kilbourne AM, Post EP, Nossek A, Sonel E, Drill LJ, Cooley S, et al. Service delivery in older patients with bipolar disorder: a review and development of a medical care model. *Bipolar Disorders* 2008;10:672–683. [PubMed: 18837861]
- Kilbourne AM, Rofey DL, McCarthy JF, Post EP, Welsh D, Blow FC. Nutrition and exercise behavior among patients with bipolar disorder. *Bipolar Disorders* 2007;9:443–452. [PubMed: 17680914]
- Kupfer DJ. The increasing medical burden in bipolar disorder. *Jama* 2005;293:2528–2530. [PubMed: 15914754]
- Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet* 1997;349:1436–1442. [PubMed: 9164317]
- Murray DP, Weiner M, Prabhakar M, Fiedorowicz JG. Mania and mortality: why the excess cardiovascular risk in bipolar disorder? *Current Psychiatry Reports* 2009;11:475–480. [PubMed: 19909670]
- Newcomer JW, Hennekens CH. Severe mental illness and risk of cardiovascular disease. *Jama* 2007;298:1794–1796. [PubMed: 17940236]
- Peele PB, Xu Y, Kupfer DJ. Insurance expenditures on bipolar disorder: clinical and parity implications. *American Journal of Psychiatry* 2003;160:1286–1290. [PubMed: 12832243]
- Rejeski WJ, Gauvin L, Hobson ML, Norris JL. Effects of baseline responses, in-task feelings, and duration of activity on exercise-induced feeling states in women. *Health Psychology* 1995;14:350–359. [PubMed: 7556039]
- Roshanaei-Moghaddam B, Katon W. Premature mortality from general medical illnesses among persons with bipolar disorder: a review. *Psychiatric Services* 2009;60:147–156. [PubMed: 19176408]
- Simon GE, Ludman EJ, Bauer MS, Unutzer J, Operskalski B. Long-term effectiveness and cost of a systematic care program for bipolar disorder. *Archives of General Psychiatry* 2006;63:500–508. [PubMed: 16651507]
- Simon GE, Unutzer J. Health care utilization and costs among patients treated for bipolar disorder in an insured population. *Psychiatric Services* 1999;50:1303–1308. [PubMed: 10506298]
- Taylor AH, Faulkner G. Inaugural editorial. *Mental Health and Physical Activity* 2008;1:1–8.
- Thayer, RE. *The origin of everyday moods: managing energy, tension, and stress*. Oxford University Press; New York, NY: 1996.
- Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Medicine & Science in Sports & Exercise* 2008;40:181–188. [PubMed: 18091006]
- Wright KA, Everson-Hock ES, Taylor AH. The effects of physical activity on physical and mental health among individuals with bipolar disorder: A systematic review. *Mental Health and Physical Activity* 2009;2:86–94.