Exercise Interventions to Augment Psychopharmacology

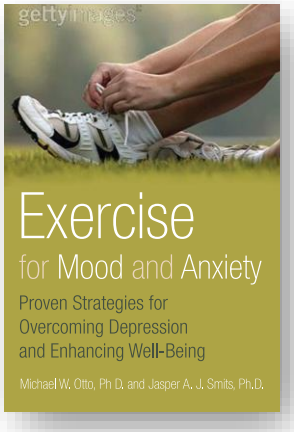
Michael W. Otto, PhD

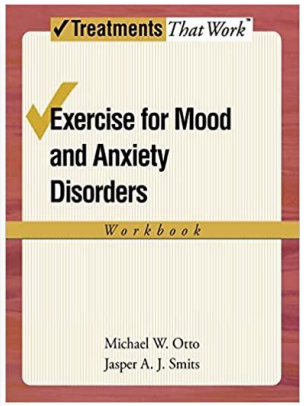
Department of Psychological and Brain Sciences, Boston University

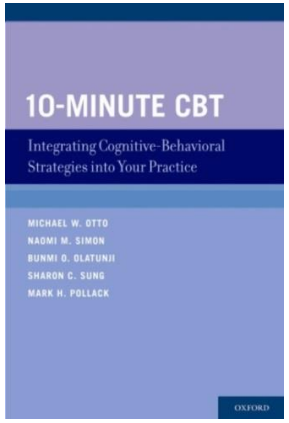
Disclosures

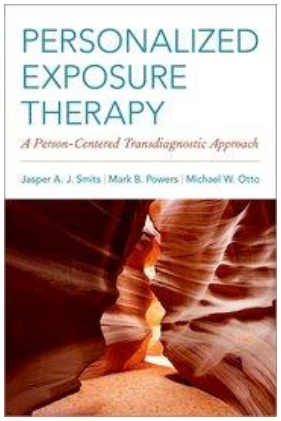
I have the following relevant financial relationship with a commercial interest to disclose:

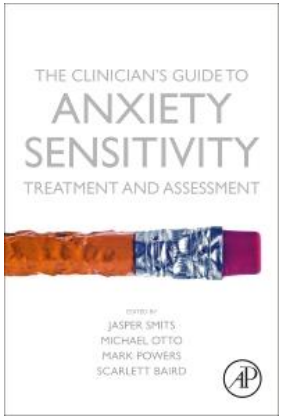
- Scientific Advisory Board Chair – *Big Health*
- Book Royalties - *Oxford, Routledge*

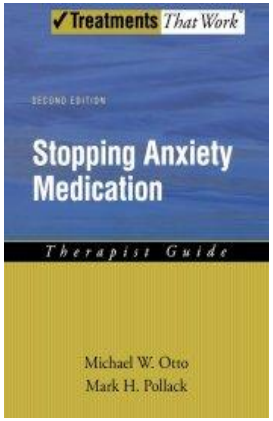


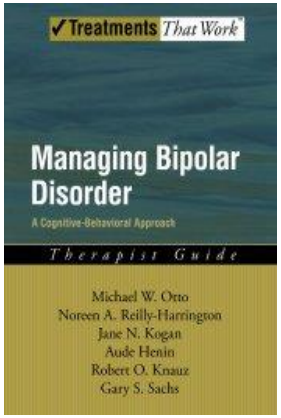


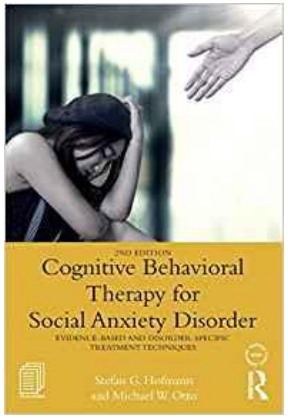












Free Stuff

Psychology Today

- http://www.psychologytoday.com/blog/exercise-and-mood

The Core

Moderate Exercise is a terrific augmentation strategy. Exercise:

- Improves mood
- Treats depression
- Treats anxiety and anxiety disorders
- Improves cognition
- Enhances sleep

- In short, prescribing exercise is a wonderful way to achieve a range of beneficial outcomes...with the side effect of living longer

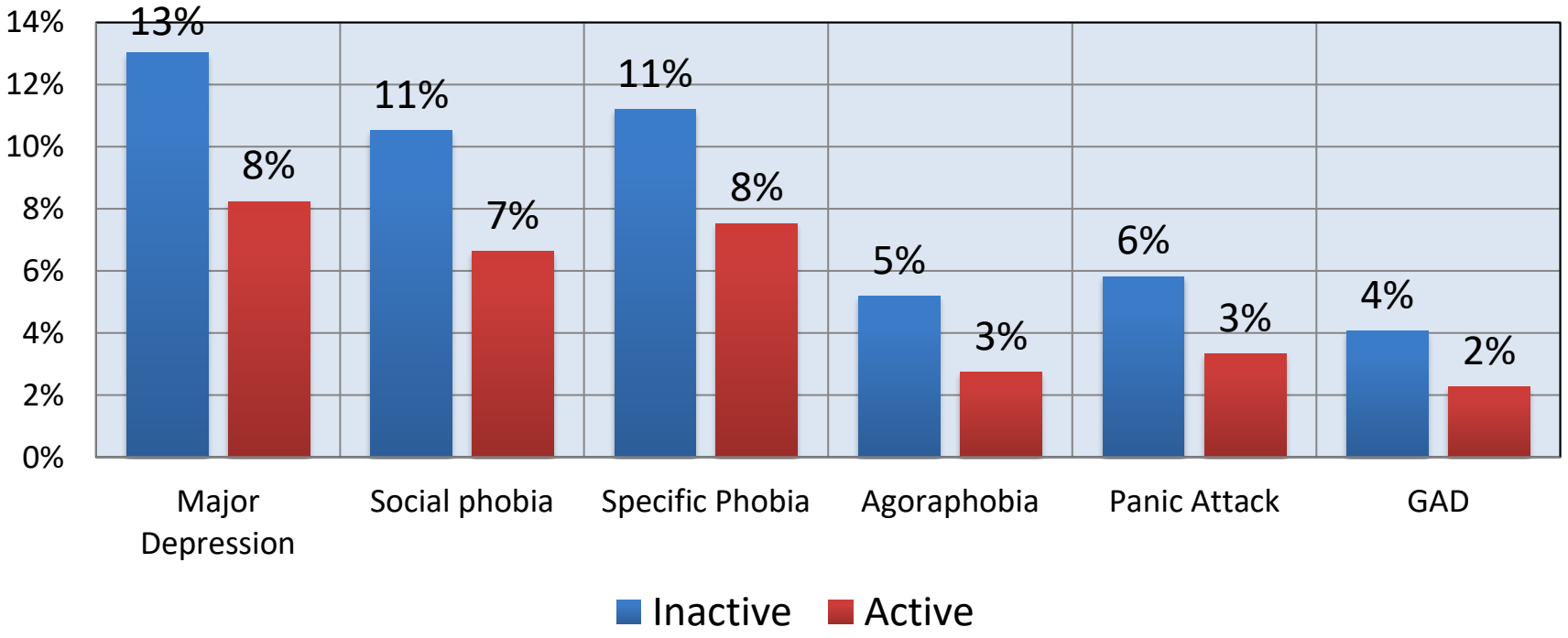
WHY PRESCRIBE EXERCISE?

Psychological correlates of exercise

- Fewer symptoms of depression
- Fewer symptoms of anxiety
- Less anger
- Less cynical distrust
- Stronger feelings of social integration

Stephens. Prev Med. 1988 Jan;17(1):35-47.

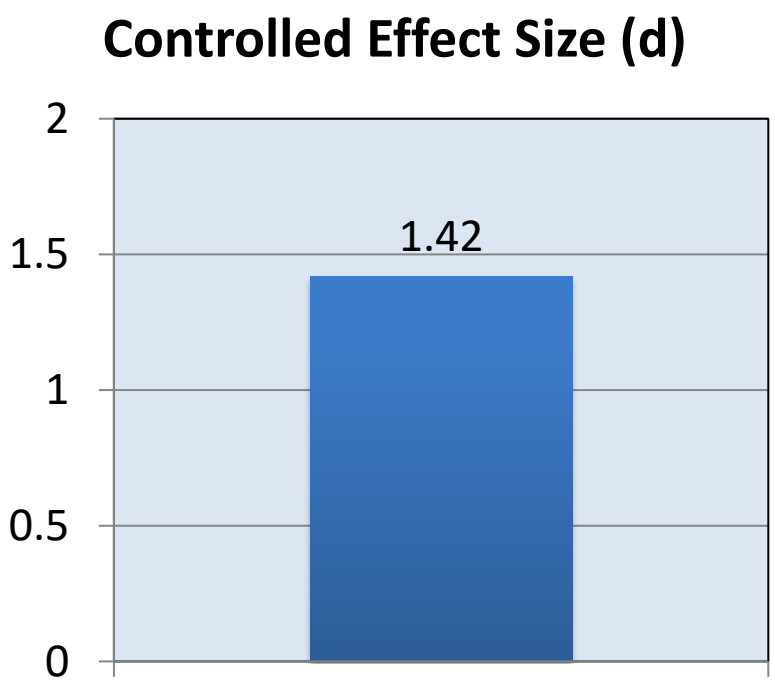
Prevalence of mood and anxiety disorders



Goodwin RD. Prev Med. 2003 Jun;36(6):698-703

Exercise for depression

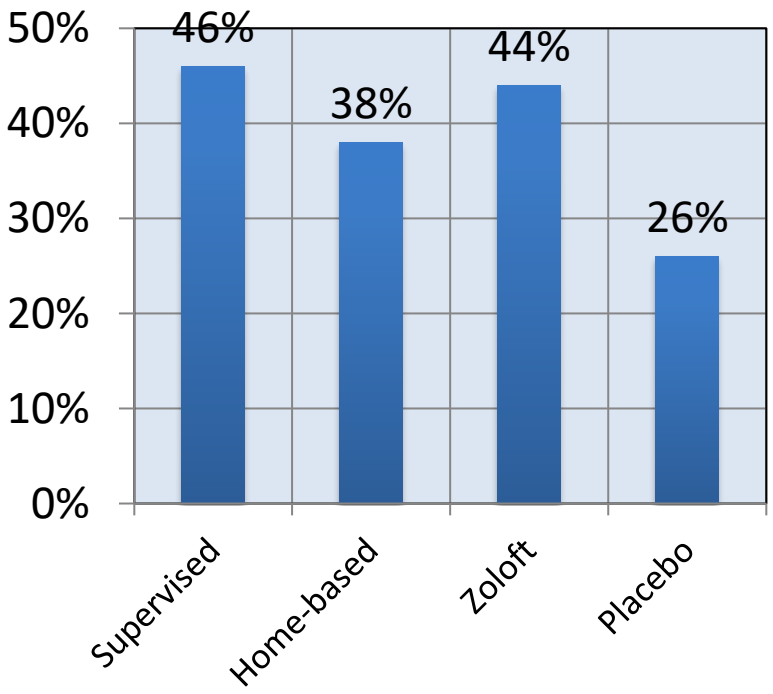
- Meta-analysis
  - 11 randomized controlled trials
    - Participants with MDD dx
    - Control = no treatment or stretching
- Intervention
  - Frequency of exercise varied from 2 to 4 times a week
  - Duration from 20 to 45 min per session
  - Intensity from being unspecified to 70–85% of the maximum heart rate



Stathopoulou et al. Clin Psychol Sci Pract. 2006; 13:179–193.

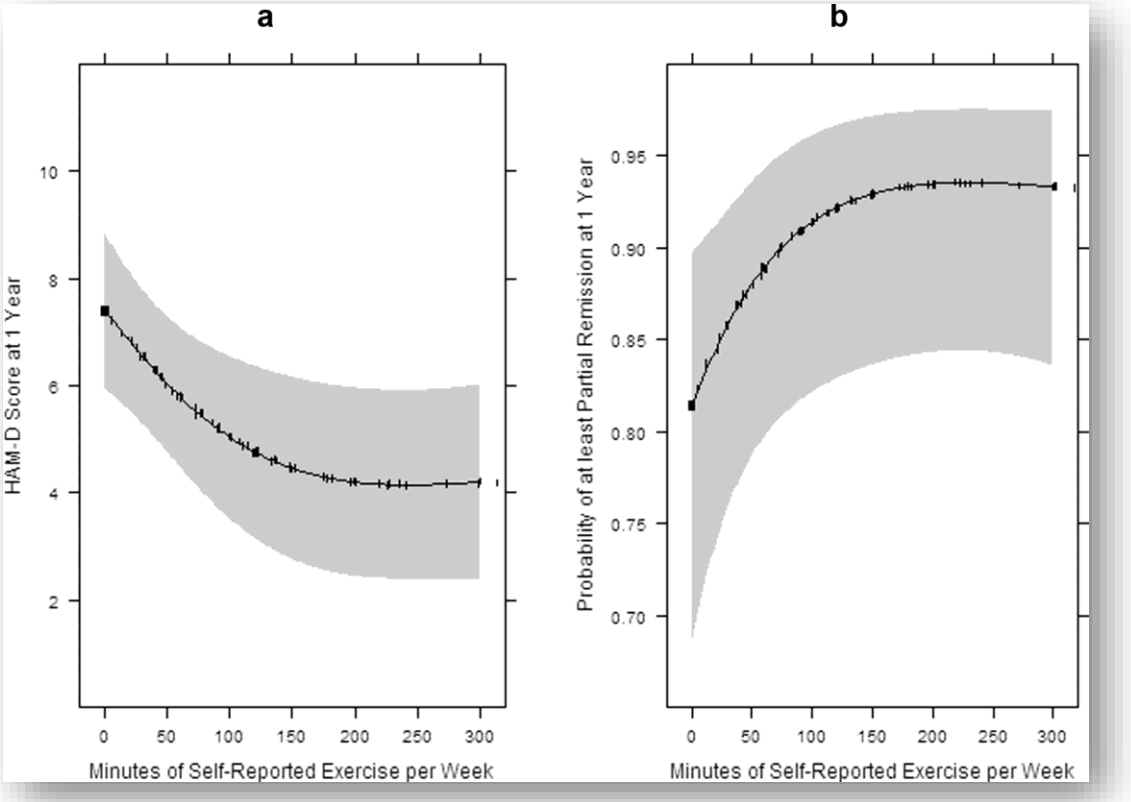
Exercise vs. Sertraline: MDD remission

- Four arms (N=202):
  - Supervised exercise
  - Home-based exercise
  - Sertraline
  - Pill placebo
- Intervention:
  - 16 weeks
  - Three 45-min sessions of vigorous-intensity exercise



Blumenthal et al. Psychosom Med. 2007 Sep-Oct;69(7):587-96.

Maintaining exercise (during 1 year follow-up period) and maintaining gains



MDD remission increased from 46% at post treatment to 66% for participants available for follow-up

Hoffman et al. Psychosom Med. 2011; 73(2):127-33.

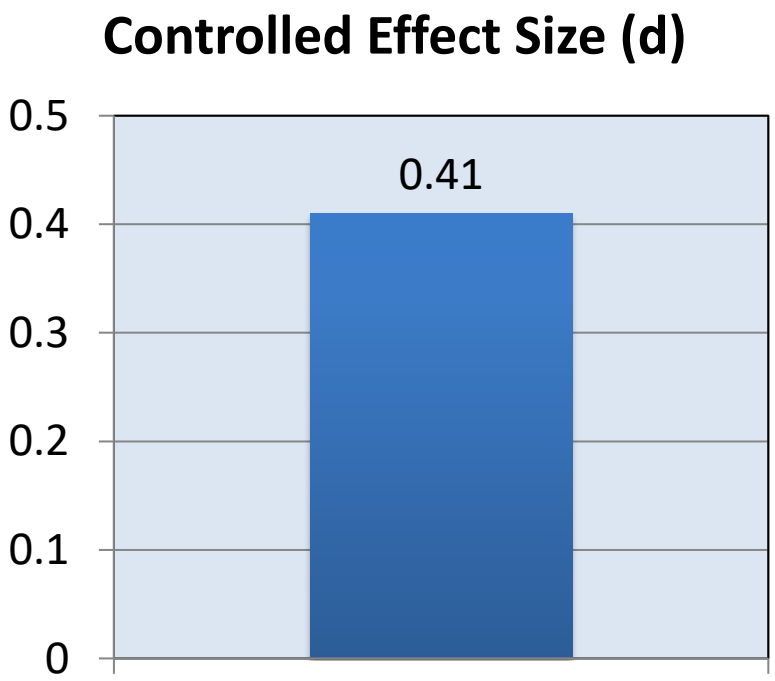
Treatment Resistant Depression

- 33 patients with treatment-resistant depression (failed 2 adequate antidepressant trials), randomized to exercise or control. Medications were continued.
- Exercise Dose: 30-40 minutes walking, 5 times a week, 12 week trial
- Support for only one of these sessions per week, reminders
- No change in stretching control group
- 10 of 19 showed response/remission

Mota-Pereira et al. (2011) Journal of Psychiatric Research, 45, 1005-1011

Exercise for anxiety

- Meta-analysis
  - 15 studies (675 patients)
    - Dx (N=9) or elevated anxiety (N=6)
    - Control = wait list
- Intervention
  - Frequency of exercise varied from acute bout to 5 times a week
  - Duration from 30 to 90 min per session
  - Intensity from moderate to vigorous, with higher effect size with vigorous



Aylett et al. BMC Health Serv Res. 2018 18:559.

Exercise for anxiety – Clinical Trials

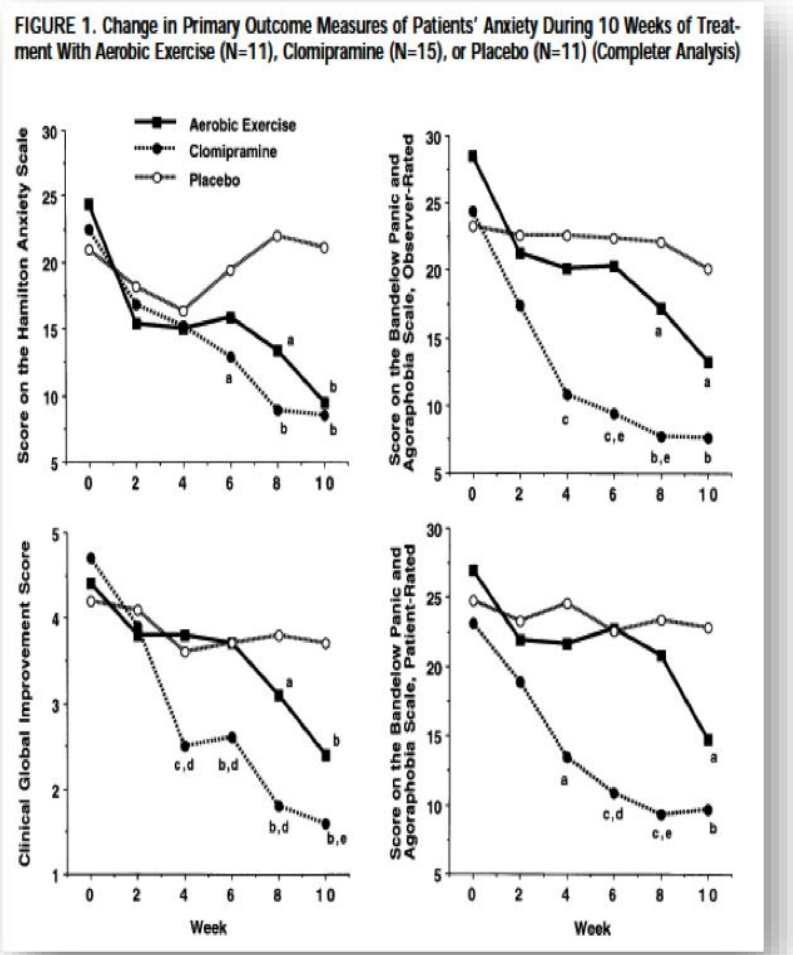
- Panic Disorder
  - Randomized trial of 46 patients (Broocks et al., 1998)
  - 3 Studies of Anxiety Sensitivity
- OCD
  - Open trial of regular exercise (Brown et al., 2007)
    - Acute gains, maintenance 6 months
- PTSD of inpatient adolescents
  - Open trial evidence (Diaz & Motta, 2008; Newman & Motta, 2007)

Randomized Trials of Adjunctive Treatment

- Outpt 8-10 week Group CBT combined with Exercise or Healthy Eating Education (Mermon et al., 2008)
  - Panic, GAD, Social Phobia
  - 150 minutes exercise across week
  - Lower anxiety, depression, and stress
- Inpatients with Panic, GAD, or Social Phobia (Martinsen et al., 1989)
  - Randomized to aerobic exercise or strength training
  - Both groups improved

Exercise for panic disorder

- Three Arms (N=46)
  - Exercise
  - Clomipramine
  - Placebo
- Intervention
  - 10 weeks
  - Exercise included completing a 4-mile route three times a week

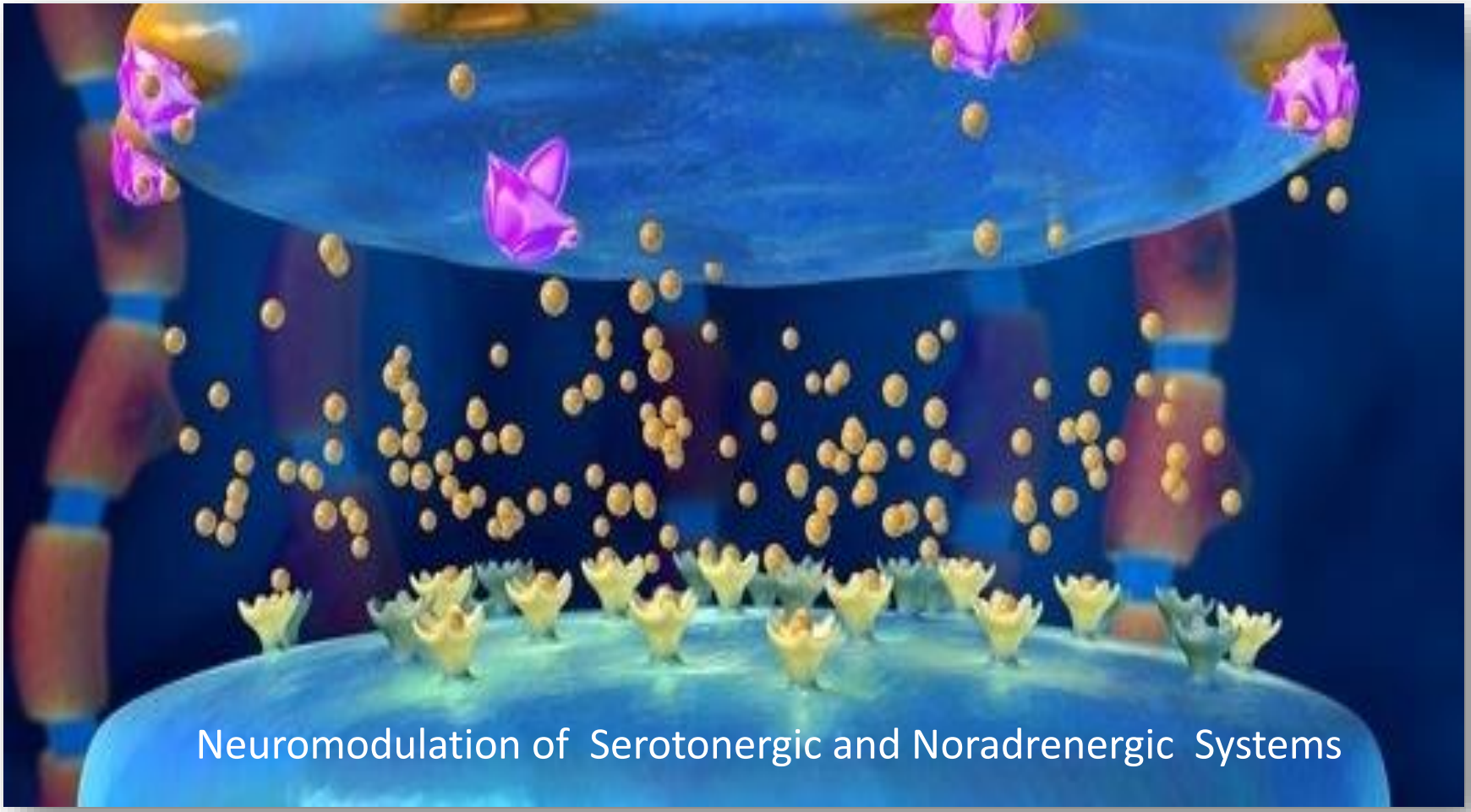


Broocks et al. Am J Psychiatry. 1998 May;155(5):603-9.

MECHANISMS UNDERLYING THE EFFECTS OF EXERCISE

Tentative Answers

Nondrug equivalent of antidepressants?



Chaouloff. Med Sci Sports Exerc. 1997 Jan;29(1):58-62.

Exercise and BDNF

- 120 Older Adults (age 55 to 80) Randomized
- Exercise vs. Stretching Control
- Dose: Walking 40 min, 3 X week
- Results
  - Enhanced BDNF
  - Reversed loss of anterior hippocampal volume
  - Link BDNF and change in volume and memory functions

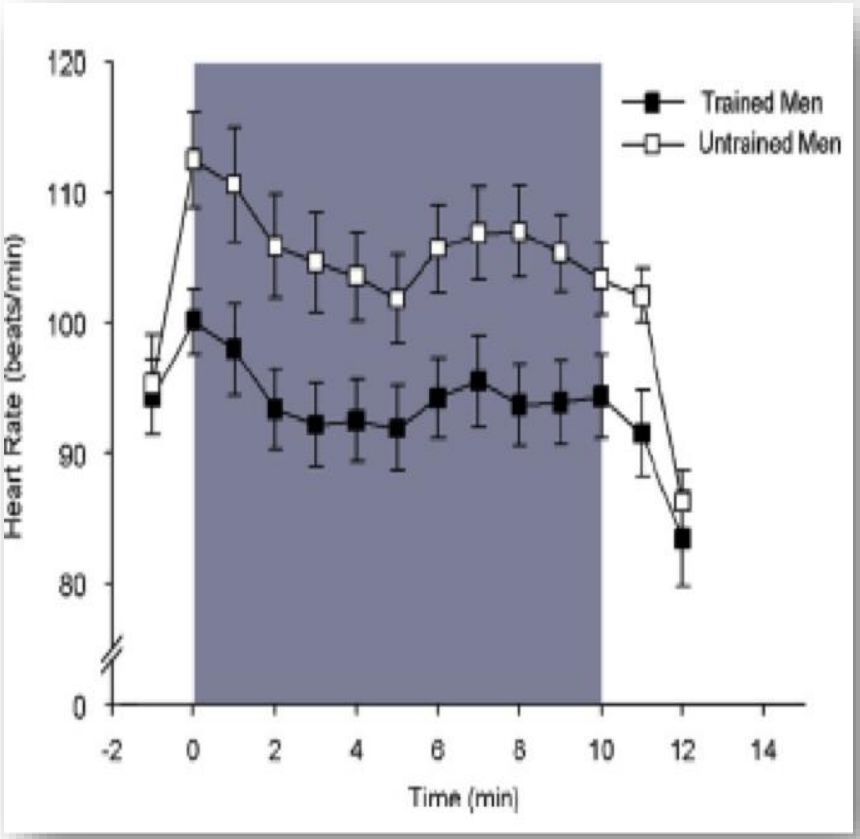
Erickson et al. 2011, PNAS, 108 (7), 3017-3022

Buffering the effects of stress

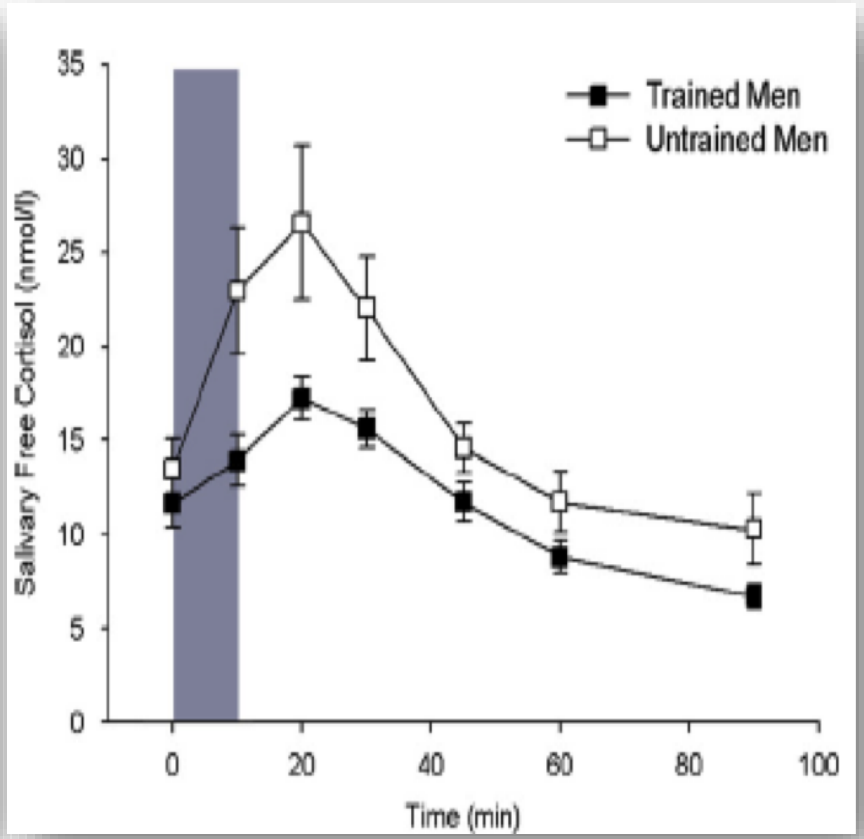
Forcier et al. Health Psychol. 2006 Nov;25(6):723-39.

Exercise and psychosocial stress reactivity

Heart Rate



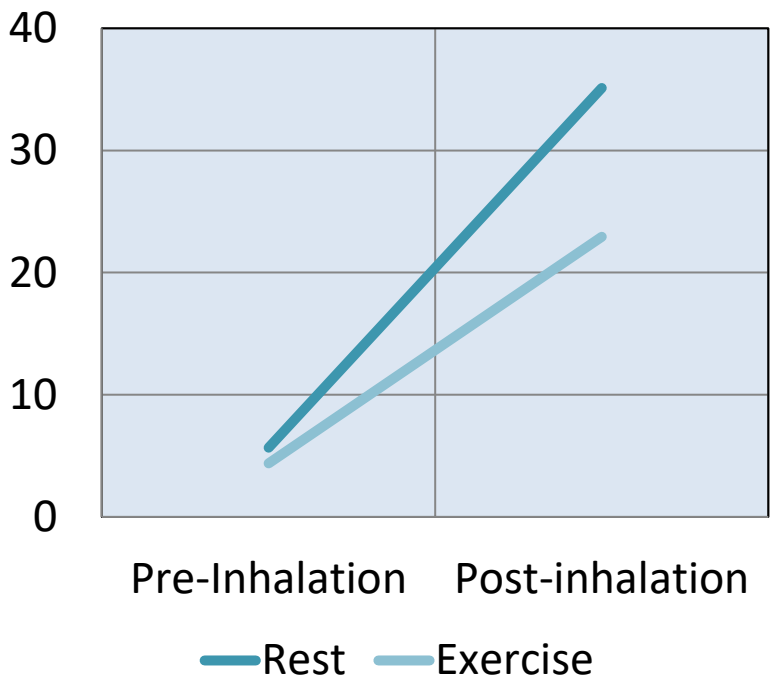
Cortisol



Rimmele et al. Psychoneuroendocrinology. 2009 Feb;34(2):190-8.

Exercise and response to CO_2 challenge

- Participants (N = 92) were 51 female and 41 male volunteers ranging in age from 17 to 24. No history of panic attacks
- Randomized to:
  - Treadmill exercise (i.e., 70% of HR_{max})
  - Quiet rest
- Single vital capacity inhalation of 35% CO2/65% O2.



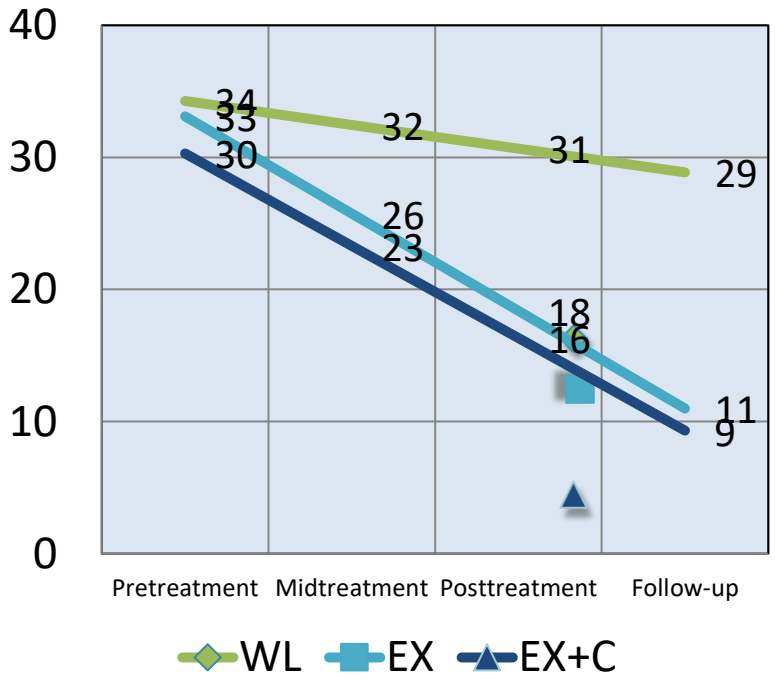
Smits et al. J Psychiatr Res. 2009 Jan;43(4):446-54.

Learning to tolerate distress and somatic arousal

- Repeated exposure to somatic arousal reduces anxiety sensitivity (fear of anxiety and related sensations) and is effective for the treatment of panic and related disorders
- Exercise induces somatic arousal akin to anxiety/stress (e.g., heart racing, rapid breathing, sweating)
- Exercise = Interoceptive exposure

Exercise reduces anxiety sensitivity or the “fear of fear”

- Sample
  - 60 volunteers
  - Clinical levels of Anxiety Sensitivity (ASI>25)
  - Sedentary
- Random Assignment:
  - Exercise (Extinction learning rationale)
  - Exercise (Extinction learning rationale) + Cognitive restructuring
  - Waitlist
- Assessments at Baseline, Midtreatment, Posttreatment, and 3-week Follow-up



Smits et al. Depress Anxiety. 2008;25(8):689-99

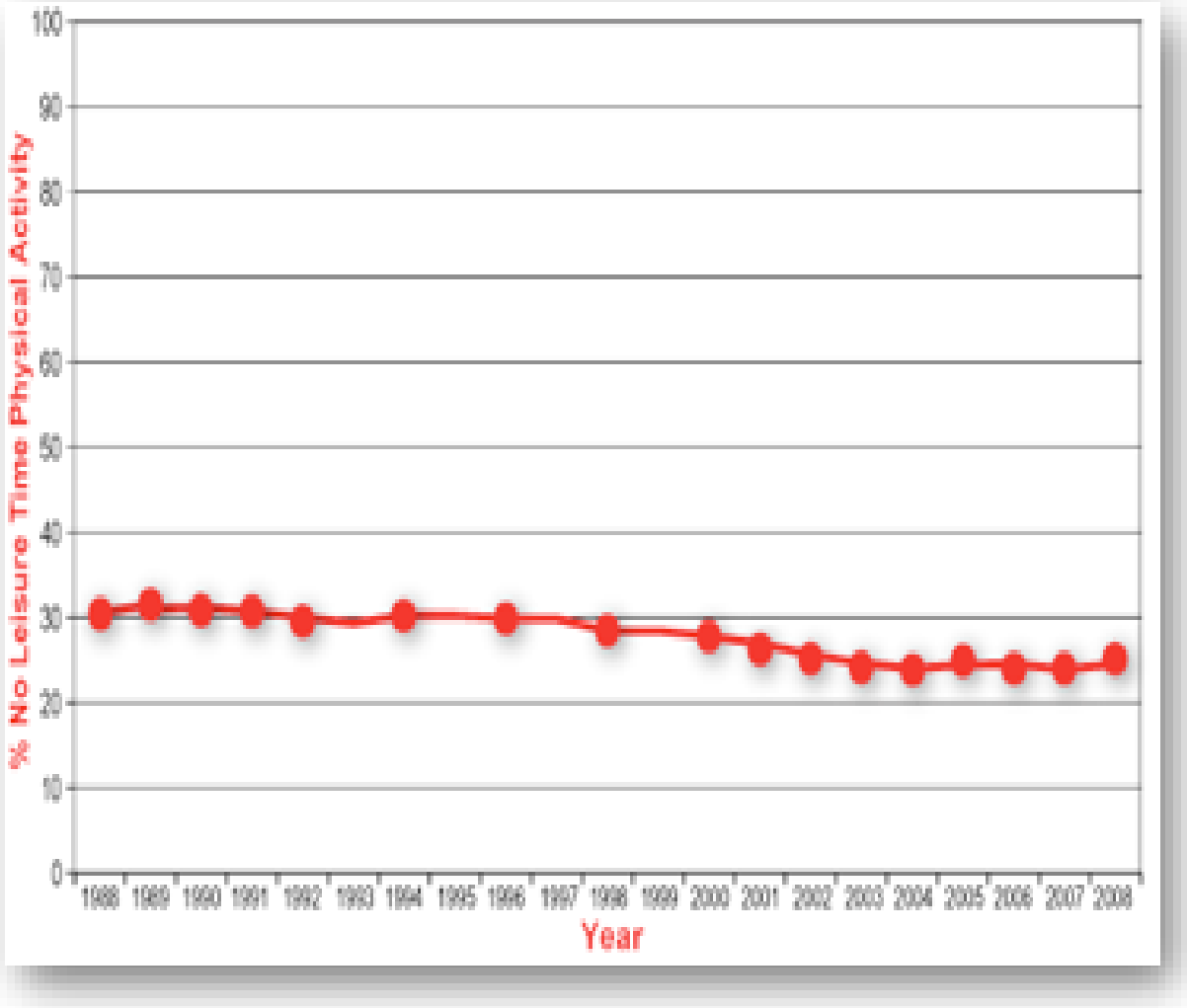
Countering maladaptive emotion action tendencies

- Replace the maladaptive action tendencies of depression (i.e., passivity) with functional actions (i.e., activation), thereby helping the patient re-establish adaptive positive activities.
- Exercise = behavioral activation

NICE MODELS AND EFFICACY

But……

We know we should exercise, yet…



THE FOREST BEFORE THE TREES

The truth about motivation

Motivation for what?

Motivation for outcome

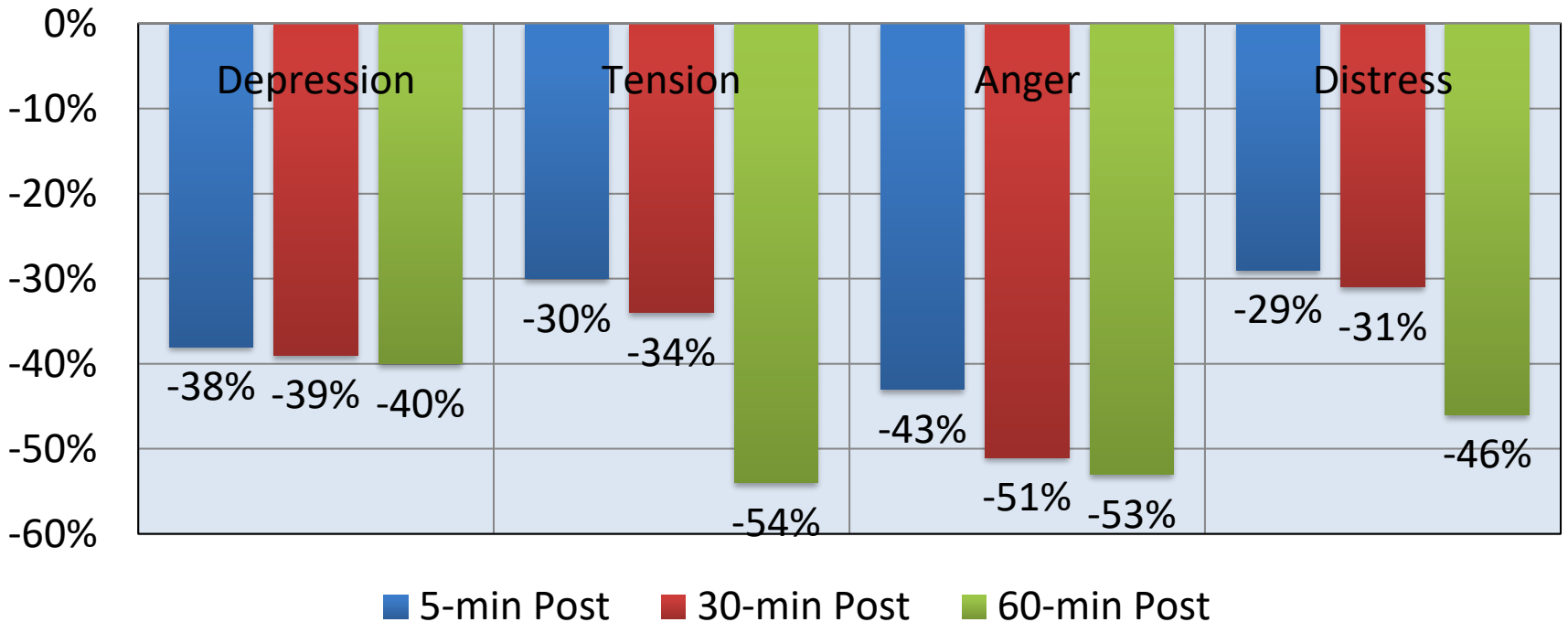
Motivation for process or effort to get there

Tight linkage between exercise and mood boost

Health boost = takes a while

Mood boost = immediate

Immediate mood boost with exercise in MDD



Bartholomew et al. Med Sci Sports Exerc. 2005 Dec;37(12):2032-7

MOTIVATIONS ARE NOT FIXED

Motivations are not fixed

Cultural Notions - Motivation , an inward reservoir

- Level of motivation (as if the tank were either full or empty)
- Waiting for motivation (as if it were an annoyingly late 3:15 train)
- Digging deep to find motivation (like drilling a new well and hoping for a gusher)

- Instead: A Hierarchy of Competing Motivations
  - Which one wins depends on external and internal context

Hierarchy of competing motivations

Carver, C. S., & Scheier, M. F. (2008). Feedback processes in the simultaneous regulation of action and affect. In J. Y. Shah and W. L. Gardner, Handbook of Motivational Science. New York: Guilford.

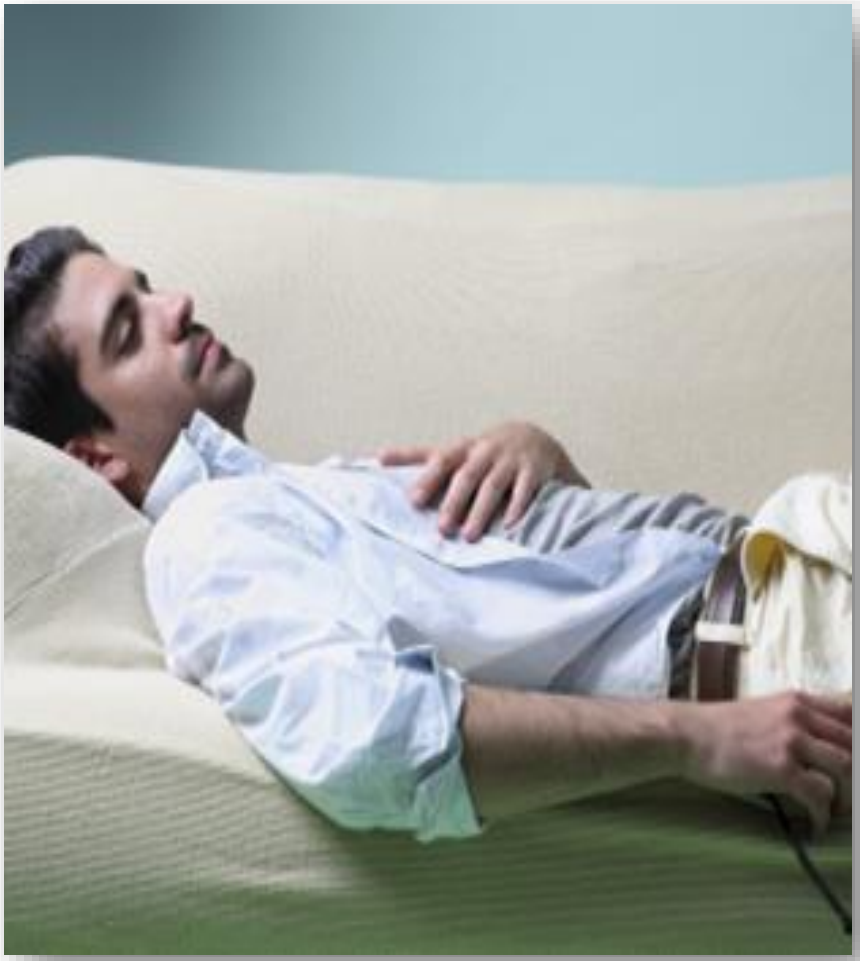
When there is space between motivation for outcome and process

- The internal push to do something
- The “effort muscle” used throughout the day:
  - No fries at lunch
  - Dealing with conflict at work
  - Paying bills at night
- A muscle that fatigues across use and is influenced by stress
- Conserve the muscle by using chaining

Muraven & Baumeister. Psychological Bulletin. 2000;126:,147-259.

USING YOUR ENVIRONMENT TO MANIPULATE YOUR HIERARCHY OF MOTIVATIONS

Mini-efforts – chaining small efforts



Hard way to get yourself to exercise:

Couch → Running

"I need to run...I need to run...I need to run"

Easier way to get yourself to exercise

Couch

"Let me just get dressed"

Running clothes on

"Now that I am dressed, let me get out of the door"

Outside

"Now that I am outside, I am going to walk a block"

Walking

"I am warmed up; I might as well jog"

Running

Manipulating motivation

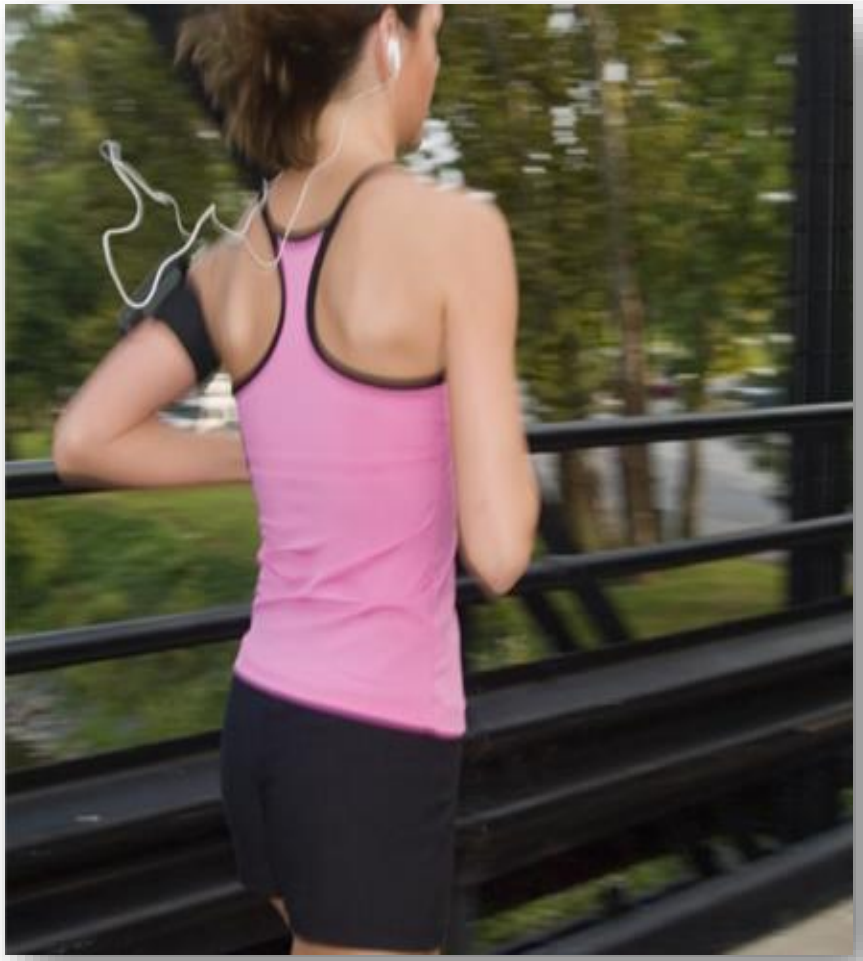
- Whenever possible combine motivations

Does it work?

- Spillage reduced by 85%

Manipulating my environment to support exercise

- I value my reading time, therefore I will only read while I run:
  - Books on tape



Cognitive coaching - addressing negative thinking

Potential goal contagion

What do I say?

- I want to feel fit like that
- I bet they are having a good time; maybe I should go running

OR

- I will never look like that
- I am so out of shape; it would be embarrassing if I ran in public like that

Aarts, J. Dijksterhuis, A, & Dik, G. (2008). Goal contagion; inferring goals from others' actions – and what it leads to. In J. Y. Shah and W. L. Gardner, Handbook of Motivational Science. New York: Guilford.

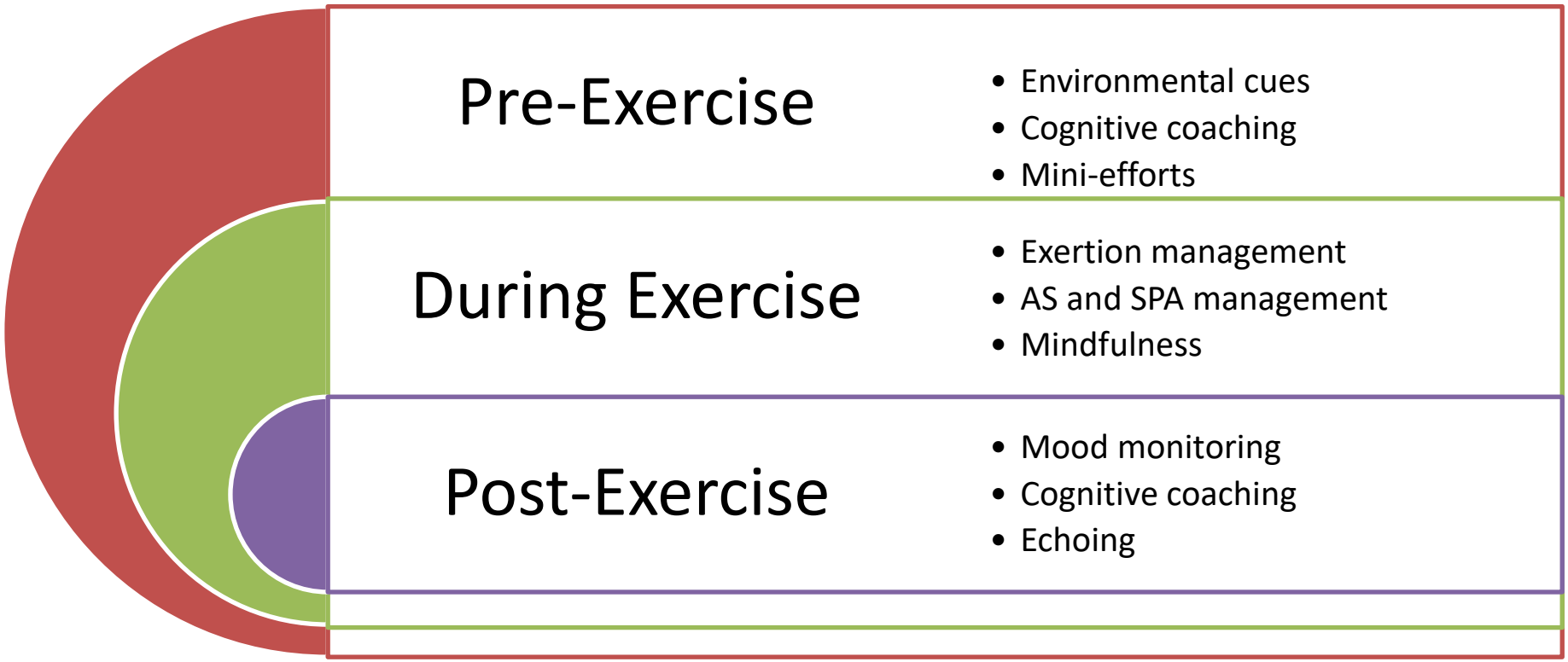
Other useful thinking strategies for exercise

- The application of restructuring to exercise diverting thoughts:
  - Pre-identification of thoughts
  - Rehearsal of countering strategies
  - Use of adaptive thinking patterns

Preparing for morning exercise

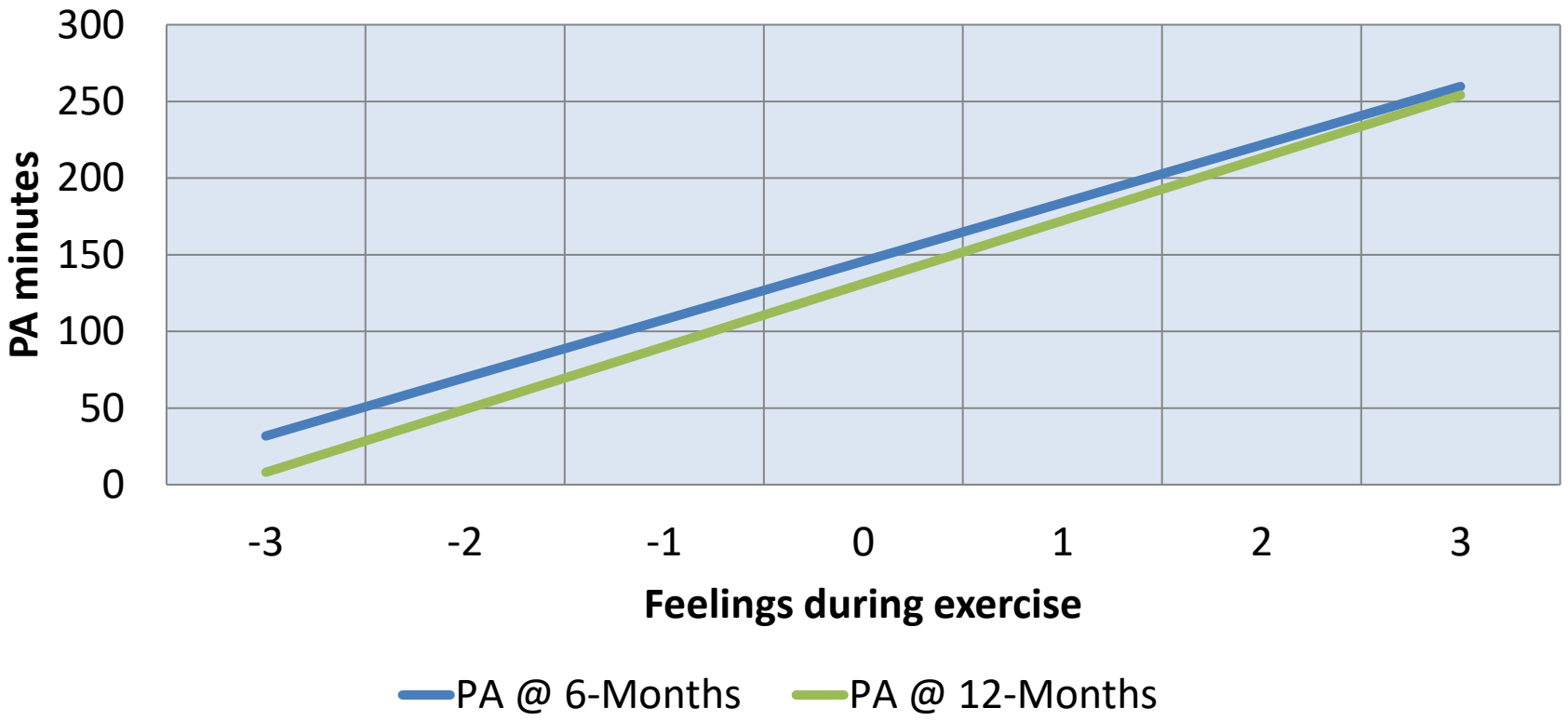
- Negative thoughts:
  - It is too cold to get out of bed
  - It well be more valuable for my mood to sleep in
  - Missing my workout this once time won't matter
  - I am too tired to exercise well
- Adaptive thought:
  - Don't let an asleep mind trump an awake mind's decision

Intervening at every stage



INTERVENING DURING EXERCISE

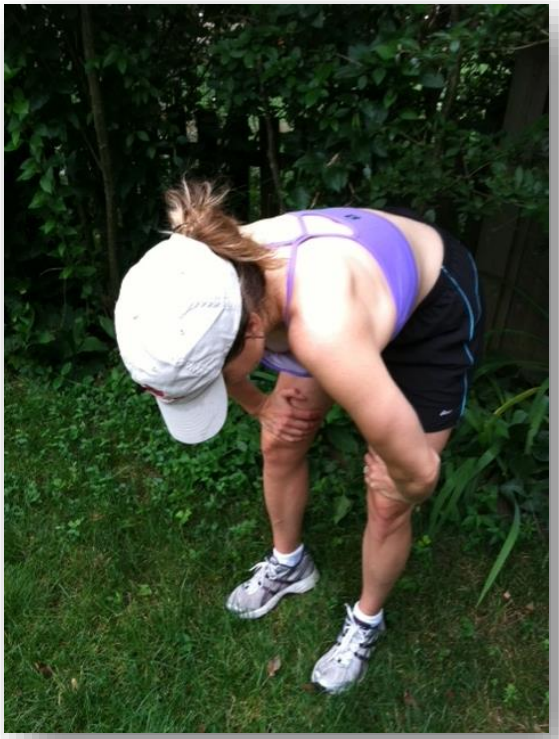
Feeling Bad During Exercise Matters



Williams et al. Psychol Sport Exerc. 2008 May;9(3):231-245.

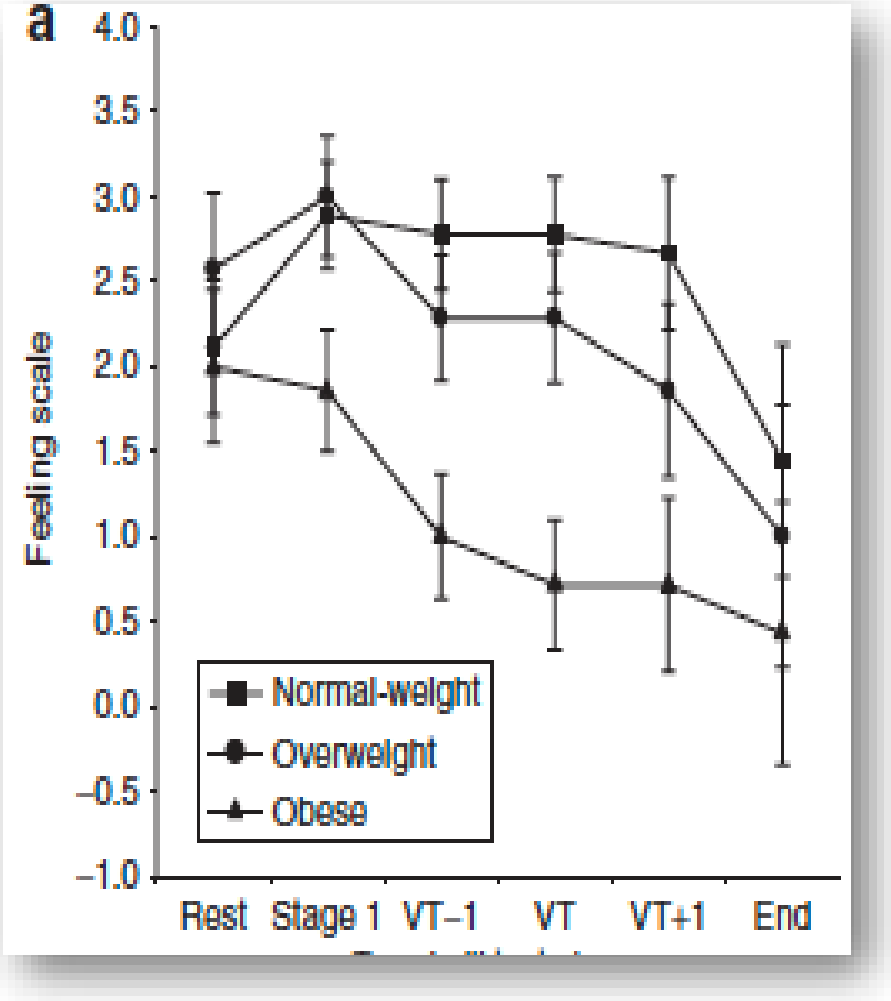
What explains feeling bad during exercise?

- Intensity too high?



Intensity matters, especially if you are not fit

- As intensity increases feelings change
  - Normal-weight
  - Overweight
  - Obese



Ekkekakis et al. Obesity. 2010 Jan;18(1):79-85.

Setting and intensity matter

Social physique anxiety (SPA)

- Rests on the assumption that others take notice of your body when you exercise and that they care enough to judge it negatively.
- The higher the SPA, the more uncomfortable a workout when other people are around, particularly if a mirror is present.

Anxiety sensitivity (AS)

- Refers to fears (and catastrophic interpretations of) somatic sensations of autonomic arousal
- Enhances the averseness of sensations of exertion

Making exercise fun

Enhance well-being strategies around exercise

Increasing the Positives

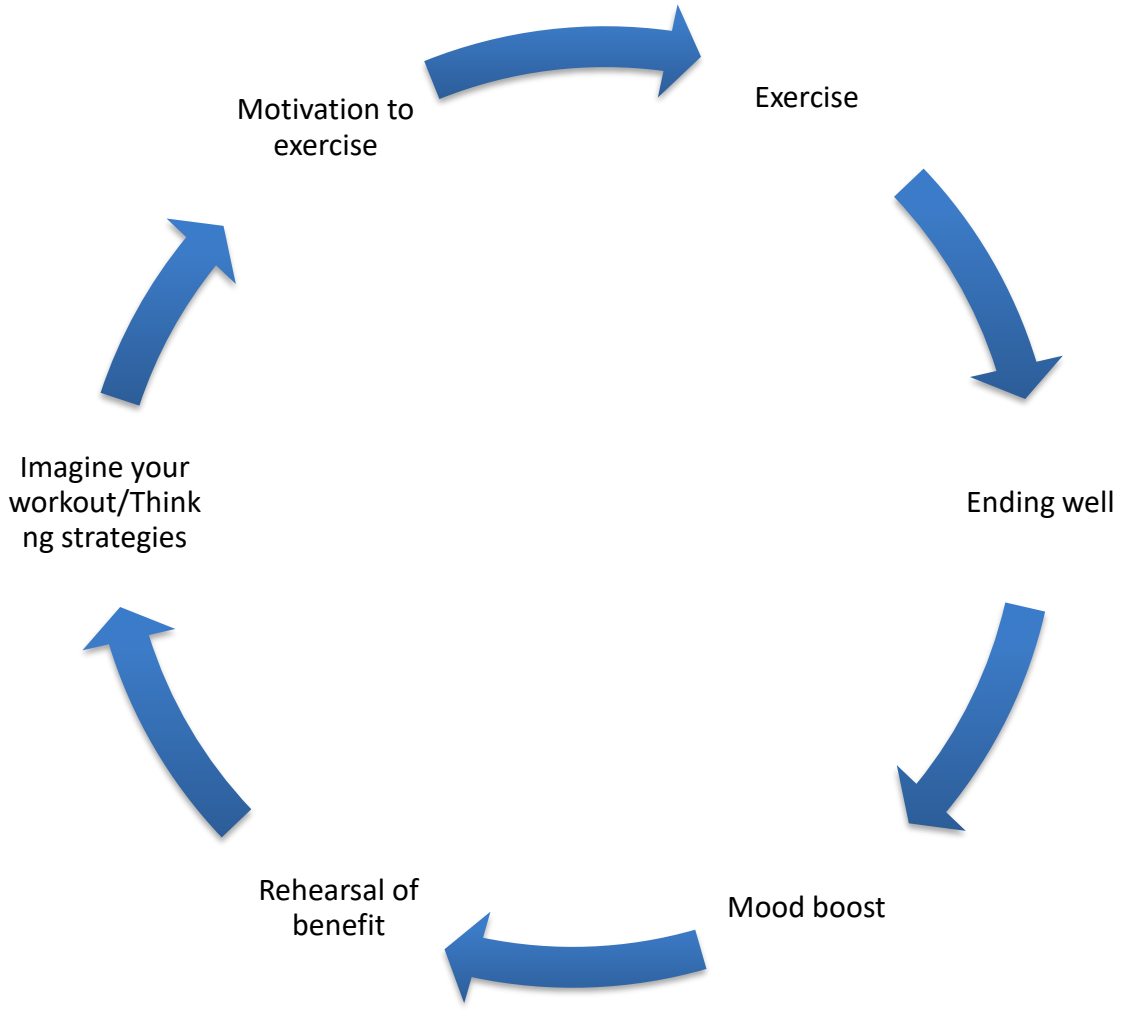
- Mindfulness
  - e.g., feel breeze
  - Notice colors
  - Music
- Finish well (recency effects on preference)
- Memory effects (picturing exercise accurately)

INTERVENING POST-EXERCISE

Rehearsal of benefit

- Wow. I did it.
- That was hard, but I feel good now.
- I have to remember how good I feel now.
- Echoing…..hours after exercise
  - I can still feel fatigue: I gave myself a good workout today
  - I am doing well, I got in 3 exercise sessions this week. I will feel this benefit.

Creating a positive cycle



THE EXERCISE PRESCRIPTION

Risk stratification

Initial ACSM Stratification	Description
Low risk	Younger individuals (<45 men; <55 women) who are asymptomatic and meet *no more than one risk factor
Moderate risk	Older individuals (men ≥45; women ≥55) or those who meet the threshold for *two or more risk factors
High risk	Individuals with one or more signs/symptoms suggestive of cardiovascular, pulmonary, or metabolic disease.

Coronary artery disease risk factor thresholds

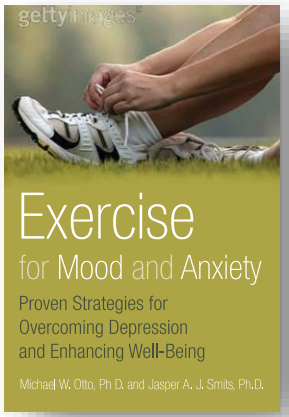
Risk Factors for CAD	Defining Criteria
Family history	Myocardial infarction, coronary revascularization, or sudden death before 55 years of age in father or other male first-degree relative or before 65 years of age in mother or other female first-degree relative
Cigarette smoking	Current cigarette smoker or those who quit within the previous 6 months
Hypertension	Systolic blood pressure of ≥140 mm Hg or diastolic ≥90 mm Hg, confirmed by measurements on at least 2 separate occasions, or on antihypertensive medication
Dyslipidemia	Total serum cholesterol of >200 mg/dl (5.2 mmol/L) or high-density lipoprotein cholesterol of <35 mg/dL (0.9 mmol/L), or on lipid-lowering medication
Impaired fasting glucose	Fasting blood glucose of ≥110 mg/dL (6.1 mmol/L) confirmed by measurements on at least 2 separate occasions
Obesity	Body Mass Index of ≥30 mg/m2, or waist girth of >100 cm (≈39.4 inches).
Sedentary lifestyle	Persons not participating in a regular exercise program or meeting the minimal physical activity recommendations from the U.S. Surgeon Generals' Report.

Traditional recommendations for medical examination prior to participation?

ACTIVITY/RISK for CAD	Low risk	Moderate risk	High risk
Moderate exercise	Not necessary	Not necessary	Recommend
Vigorous exercise	Not necessary	Recommend	Recommend

Then again, why not be ultra safe…

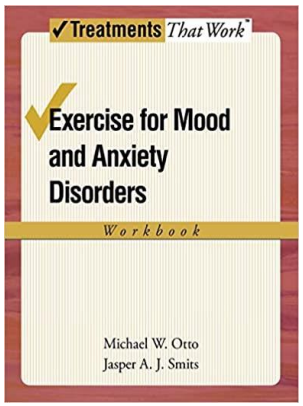
Finding the right activity (have fun)



Selecting Activities Worksheet

Check off or write in the activities that seem most fitting for your exercise interests.

Moderate-intensity exercise	Vigorous-intensity exercise
☐ Walking at 3–4 mph	☐ Jogging or running at >4.5 mph
☐ Bicycling on flat ground at 10–12 mph	☐ Bicycling on flat ground at >12 mph
☐ Swimming leisurely	☐ Swimming—moderate/hard
☐ Doubles tennis	☐ Cross-country skiing >2.5 mph
☐ Shooting baskets	☐ Rollerblading
☐ _____	☐ _____
☐ _____	☐ _____
☐ _____	☐ _____



http://www.psychologytoday.com/blog/exercise-and-mood