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A Transdisciplinary Model Integrating Genetic, Physiological, and Psychological Correlates of Voluntary Exercise

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Objective: Physical inactivity contributes to as many as 250,000 premature deaths per year (R. R. Pate et al., 1995). The authors' objective was to test a transdisciplinary model of the ways in which genetic variants, physiological factors, and psychological factors are thought to influence exercise with 64 healthy, regular exercisers. ***Design:*** In a within-subjects design, psychological and physiological responses to exercise were compared with responses to a sedentary activity. ***Main Outcome Measures:*** The authors measured affective state, perceived exertion, heart rate, and temperature change in response to moderate exercise versus sedentary activity. They also quantified genotypes on a single nucleotide polymorphism in the brain-derived neurotrophic factor (*BDNF*) gene. ***Results and Conclusions:*** The data show a relation between increases in positive affective states and acute exercise behavior, as opposed to a sedentary control. The *BDNF* gene moderated the effect of exercise on mood, heart rate, and perceived exertion. Physiological factors were, in turn, related to mood response, and mood response was a significant correlate of motivation to exercise in the future and of current exercise behavior. The model has potential as a framework for the basic study of the genetic, physiological, and psychological processes involved with voluntary exercise and as a tool for the applied examination of tailored exercise interventions and their efficacy for different subsets of individuals.

Keywords: exercise, transdisciplinary, genetics, physiology, mood

Regular physical activity has been implicated in the prevention of cardiovascular disease and of a number of cancers including those of the colon, breast, endometrium, and prostate (Friedenreich, 2001; Kaaks & Lukanova, 2002; Pate et al., 1995). Recent reports estimate that approximately 30% of total cancer deaths are related to poor exercise and nutrition, and when taking into consideration both cardiovascular disease and cancer, that inactivity contributes to as many as 250,000 premature deaths per year (Pate et al., 1995). Despite the fact that the relation between poor exercise habits and morbidity and mortality has been well understood for some time, interventions designed to promote a healthier lifestyle have largely failed to produce long-term positive results. Effective interventions to increase physical activity are sorely needed, and the development of such interventions requires conducting basic research to identify both distal and proximal determinants of voluntary physical activity. A more comprehensive understanding of the psychological, behavioral, genetic, and physiological determinants of developing and maintaining exercise behavior will inform the development of interventions that specifically target these determinants of physical activity.

One limitation of prior work in this area is the lack of an overarching theoretical framework that functionally links genetic, physiological, and psychological predictors of exercise behavior. In this research, we propose a transdisciplinary (Rosenfield, 1992) model of the ways in which genetic variants, physiological factors, and psychological factors are thought to influence exercise behavior (see Figure 1). In this broad framework, we hypothesized that the physiological effects (e.g., changes in body temperature, heart rate) of exercise influence the subjective experience of exercise (e.g., changes in mood, perceived exertion, perceived reward), which in turn are important determinants of motivation to exercise (e.g., higher self-efficacy for exercise behavior and higher intentions to exercise) and of future exercise behavior. As delineated in Figure 1, this model is both circular and dynamic. Genetic factors are included in the model as potential moderators or determinants of the physiological effects of exercise as well as the subjective experience of exercise. The implications of this model are that individuals who are better able to cope with exercise physiologically (e.g., better modulation of body temperature) will experience more of the immediate positive benefits of exercise (e.g., increases in positive mood, less perceived exertion) and develop higher motivation to exercise (e.g., greater intentions). Finally, this motivation is translated into future exercise behavior, and future exercise behavior recapitulates the model, thereby reinforcing positive experiences of exercise behavior, more positive attitudes, greater intentions, and greater self-efficacy.

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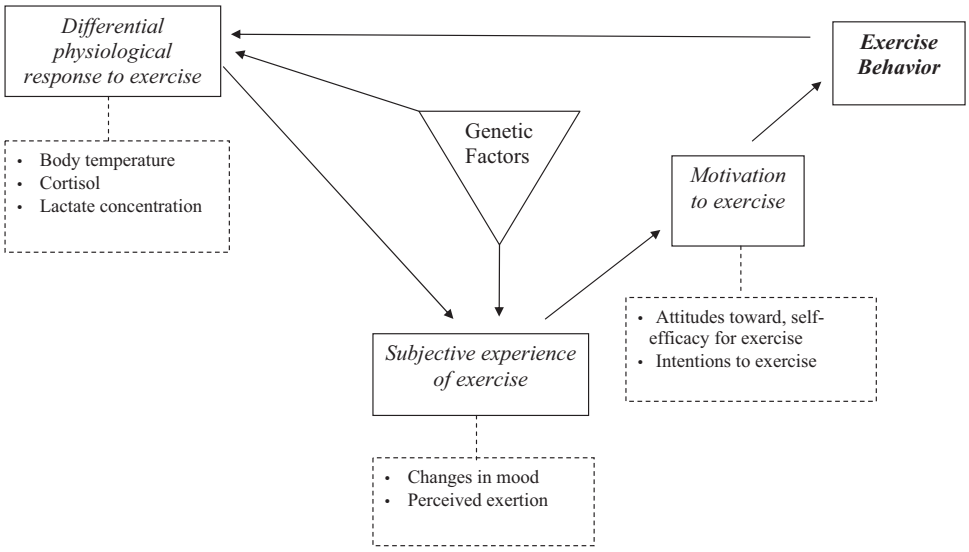

Figure 1. Transdisciplinary model of exercise behavior.

Another implication of the model is that genetic factors (or other individual differences) that influence the physiological effects of exercise or the subjective experience of those effects may also influence constructs downstream in the model (i.e., intentions, self-efficacy, motivation, and actual exercise behavior). Clearly, this model is but a starting point for what is sure to be a complicated, dynamic system that ultimately influences who engages in exercise and who remains sedentary. However, as a working model it has heuristic value and provides causal paths that can be tested empirically.

Studies have indicated that genetic factors account for approximately 29%–62% of the variance in daily exercise behavior and 35%–83% of the variance in sports participation (cf. Beunen & Thomis, 1999, or Bouchard & Perusse, 1994). Despite the clear heritability of exercise behavior, work on the human genome has only recently implicated specific genes that are related to the motivation to exercise or to the maintenance of exercise behavior. One limitation of some prior research in this area is the focus on athletic performance phenotypes (e.g., Rankinen et al., 2001). From a disease prevention perspective, the movement of sedentary individuals to some level of exercise has huge potential for reductions in morbidity and mortality, whereas improved performance among elite athletes has no such application. Further, many association studies lack a strong a priori theoretical framework that infers a causal connection between a particular genetic factor, a biological mechanism, and a behavioral outcome. In line with our model, we have identified a gene that shows promise in terms of being potentially related to endophenotypes of physiological response to exercise.

Brain-derived neurotrophic factor (BDNF) is a peptide growth factor that has broad influence on central and sensory neuronal function (Ernfors, Lee, & Jaenisch, 1994; Jones, Farinas, Backus, & Reichardt, 1994), on development of the vasculature (Donovan et al., 2000), and on neuronal growth and regeneration in the hippocampus as well as in other brain regions, in the spinal cord, and in skeletal muscle (Gómez-Pinilla, Ying, Opazo, Roy, & Edgerton, 2001; Johnson & Mitchell, 2003; Lu & Gottschalk, 2000). Recent research in both human and nonhuman animals has implicated BDNF deficits in depression and other central nervous system disorders (see Liu et al., 2005), whereas voluntary exercise increases levels of BDNF and improves cognitive performance (Cotman & Berchtold, 2002). Because the vasculature, musculature, and central nervous system are all likely critical to the ability to exercise, *BDNF* is an excellent candidate as a gene that may be associated with exercise behavior. We stress, however, that we believe there are potentially many different genetic factors associated with voluntary exercise. We chose to examine BDNF in this study as a "proof of concept" of our model, not to position it as the sole important genetic factor in voluntary exercise.

In this study, we focus on three physiological responses to exercise: (a) ratings of perceived exertion, (b) heart rate during exercise, and (c) thermoregulation during exercise (i.e., body temperature). Ratings of perceived exertion and increased heart rate are clearly important factors with respect to exercise behavior. Increases in body temperature (tympanic measure) in response to exercise appear to be strongly associated with increases in negative affect (e.g., Petruzzello, Landers, & Salazar, 1993; Smith, Petruzzello, Kramer, & Misner, 1997). Hansen, Stevens, and Coast (2001) noted that increases in room temperature were significantly associated with greater negative affect after a 30-min bout of exercise. In theory, individuals who experience greater physiological distress during exercise (i.e., greater perceived exertion, greater heart rate, and greater temperature increases) should also experience less positive affect after exercise, should find exercise to be less rewarding and reinforcing, and should demonstrate less motivation for future exercise, as compared with those who show less physiological distress.

Perhaps the most well-documented immediate benefit of exercise is psychological; acute exercise increases positive mood and decreases negative mood (Hansen et al., 2001; Yeung, 1996). The effects on mood are observed with as little as 10 min of exercise, although most studies involve approximately 30 min of exercise,

consistent with public health recommendations (e.g., Pate et al., 1995). The exertion levels of these acute bouts of exercise have ranged from 50%–75% of maximal oxygen capacity (VO_2 max; c.f. Yeung, 1996). It stands to reason that individuals who perceive an immediate mood benefit of exercise might be more likely to exercise, but several studies have failed to find an association between the effects of exercise on mood and previous exercise behavior. It is interesting to note that the few studies that have suggested an association between mood and exercise behavior have been those that utilize stronger methodologies and research designs (e.g., Boutcher & Landers, 1988; Petruzzello, Hall, & Ekkekakis, 2001). Again, previous studies have suffered from the lack of a strong theoretical framework linking the effect of exercise on mood to the motivation to exercise. Our framework suggests that the experience of increased positive mood after exercise leads to more positive attitudes, a greater sense of self-efficacy for exercise, greater intentions to exercise and ultimately higher levels of exercise behavior.

The goal of this program of research is ultimately to understand why some people exercise for at least the minimum duration and intensity recommended by public health agencies (e.g., Pate et al., 1995) and why some do not. To begin to answer this question, we examined responses to the most commonly recommended duration and intensity of exercise for general health, that is, sustained, submaximal aerobic exercise for at least 30 min (Pate et al., 1995). We operationalized this public health recommendation as a 30-min bout of aerobic exercise at 65% of VO_2 max. We compared this exercise session with a control session that consisted of watching a 30-min documentary to demonstrate that (a) a functional single nucleotide polymorphism (SNP) in the *BDNF* gene is associated with psychological and physiological response to exercise in the laboratory; (b) physiological responses involving differential exertion, heart rate, and temperature regulation predict differential positive mood response to exercise; (c) positive mood increases in response to exercise are associated with higher motivation to exercise; and (d) higher motivation is associated with greater exercise behavior.

Method

Participants

Sixty-four participants (32 men, 32 women), average age 23.8 years (range = 18–36 years), were recruited from the University of Colorado at Boulder campus community. Criteria for inclusion in the study were (a) being ages 18–36 years, (b) having no history of cardiovascular or respiratory disease, (c) being a nonsmoker, (d) not being currently on a restricted diet, (e) not having had flu or illness in the past 3 months, (f) having a body mass index (BMI) in the range of 18–29 (low-to-moderate range for adults), (g) not being currently pregnant and having a normal menstrual cycle, (h) not being diabetic, (i) not being on psychotropic medications and not currently being under treatment for any psychiatric disorder, and (j) being physically capable of engaging in moderate exercise activity (i.e., not having injuries or physical impairments).

Participants were recruited through posters advertising the opportunity to make $50 in exchange for participation in a research study on exercise. Participants who expressed interest in the study by calling the number on the flier participated in an initial screening session, during which they were provided with a detailed description of the study. Participants were then asked for their verbal consent to proceed with the phone screening and were assessed for the aforementioned exclusionary criteria. Participants had to be currently participating in some level of exercise but were excluded if they were elite athletes. On average, participants exercised 3–4 days per week. If the participants met study criteria, they were invited to the Boulder General Clinical Research Center, where they signed an informed consent form before participating. All procedures were reviewed and approved by the University of Colorado at Boulder internal review board as well as by the University of Colorado Health Sciences Center Scientific Advisory Committee, which oversees the Boulder General Clinical Research Center.

Procedure

There were three total laboratory sessions. The first session included the participants' completing informed consent documents, having baseline measures taken, and engaging in a test of aerobic exercise capacity (VO_2 max). Consistent with established procedures (Christou, Gentile, DeSouza, Seals, & Gates, 2005), VO_2 max was assessed via online computer-assisted open-circuit spirometry during incremental treadmill exercise. Each participant engaged in a 6- to 10-min warm-up period and then ran or walked at a comfortable speed that corresponded to 70%–80% of age-predicted maximal heart rate. The treadmill grade was increased 2.5% every 2 min until volitional exhaustion. For a valid VO_2 max, each participant had to meet at least three of the following four criteria: (a) plateau in VO_2 max with increasing exercise intensity, (b) a maximal respiratory exchange ratio of $\geq$1.15, (c) achievement of age-predicted maximal heart rate ($\pm$10 beats per minute), and (d) a rating of perceived exertion of $\geq$18 on the Borg (1985) scale.

Participants were asked to come to all sessions in loose-fitting clothing or exercise attire and to wear athletic shoes. They were instructed to eat and drink normally and to not consume alcohol during the 24 hr prior to testing. The first experimental session was scheduled 1 week after the VO_2 max session. At the first experimental session, participants completed the preactivity questionnaire and were then randomly assigned (within gender) to either the exercise condition or the control condition. Participants were then moved to either the exercise room (containing a treadmill) or the control room (containing a comfortable chair, television, and VCR). Participants in the exercise condition were asked to warm up on the treadmill until they achieved 65% of their previously measured VO_2 max. Once participants achieved 65% VO_2 max, they were asked to maintain this level of exertion for 30 min. In the control condition, participants viewed a 30-min documentary on bookbinding that was informally pilot tested prior to the study to ensure that it was a neutral emotional stimulus.

Participants in both conditions had their body temperature and mood sampled at baseline, 5 min, 10 min, and 20 min into the testing session. Immediately after the activity session, participants completed posttest mood measures and measures of heart rate and body temperature. The second session took 1.5 hr. The third session was scheduled 1 week after the second session. All procedures in the third and final session were identical to the procedures in the second session except that participants engaged in whichever activity they did not complete at the second session (i.e., sedentary or exercise). The order of the sessions was thus counterbalanced across participants, such that half the participants received acute exercise first and half received the sedentary control condition first. Order of sessions did not influence our results.

Baseline Measures (Session 1)

Motivation. Our measures of motivation were derived from the theory of planned behavior (TPB; Ajzen, 1991; see Bryan & Rocheleau, 2002), in which attitudes toward exercise are measured with four items targeting outcome expectancies regarding exercise (e.g., "Exercise would make me healthy," α = .79). Norms items (k = 6) including perceived normative support as well as descriptive norms for exercise also formed a reliable scale (α = .82). Self-efficacy is also measured in standard TPB format with

seven items that reflect the extent to which participants feel confident in their ability to engage in aerobic exercise ($\alpha = .81$). Intentions to engage in aerobic exercise ($k = 4$) assesses the likelihood of exercise behavior in the next 3 months ($\alpha = .75$). The TPB has demonstrated reliability and validity in predicting exercise behavior and maintenance (Armitage, 2005; Hagger, Chatzisarantis, & Biddle, 2002).

Exercise history. Level of voluntary exercise was assessed with three questions specifically targeting voluntary aerobic exercise (Bryan & Rocheleau, 2002). Participants were given a definition of aerobic exercise, that is, "Any activity that uses large muscle groups and is done at a level that causes your breathing to be heavy and your heart to beat faster (examples are running, swimming, bicycling, step aerobics, basketball)." Participants were then asked, (a) in the past 3 months how often they engaged in any aerobic activity for 30 min or more, (b) in the past 3 months what is the average number of days per week that they engaged in aerobic exercise for 30 min or more, and (c) in the past 7 days only, how many days did they engage in aerobic exercise for 30 min or more ($\alpha = .86$).

BMI. Height and weight were measured to calculate BMI.

Experimental Session Measures (Sessions 2 and 3)

Measures of mood. We included two measures of mood, one a domain general and well-established scale and the second a newer, exercise-specific measure. The Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1971) uses bipolar adjective scales to assess mood. Four POMS dimensions (vigor, tension, depression, elation) were utilized in this research. The POMS is a domain general measure but has been widely utilized in exercise research (cf. Berger & Motl, 2000). Because of its length, the POMS was given to participants only immediately prior to and immediately following the 30-min activity. The Physical Activity Affect Scale (PAAS; Lox, Jackson, Tuholski, Wasley, & Treasure, 2000) assesses exercise-induced feeling states of positive affect, negative affect, tranquility, and physical fatigue. The PAAS was developed in response to concerns about the lack of exercise-specificity of measures like the POMS and shows adequate internal consistency and discriminant validity among the factors.

Rating of Perceived Exertion (RPE). The RPE is a subjective measure commonly used to assess exertion during exercise, has adequate reliability and validity (Borg, 1985), and is frequently used in laboratory studies of exercise (e.g., Petruzzello et al., 2001).

Heart rate. Mean beats per minute were recorded during and immediately after the exercise–sedentary activity by a Polar S610 heart monitor (Biometrics, Boulder, CO) worn continuously during the session.

Tympanic temperature. Temperature was measured by a Braun ThermoScan Pro 3000 (Braun, Kronberg, Germany). The ThermoScan measures the infrared heat generated by the eardrum and surrounding tissue. Clinical studies have shown that the ear is an excellent site for temperature measurement because temperatures taken in the ear reflect the body's core temperature (Sato et al., 1996; White, Baird, & Anderson, 1994). Body temperature is regulated by the hypothalamus, which shares the same blood supply as the tympanic membrane. Changes in core body temperature are usually seen sooner at the tympanic membrane than at other sites, such as the rectum (e.g., Newsham, Saunders, & Nordin, 2002). The PAAS, RPE, temperature, and heart rate were assessed immediately prior to, 5 min in, 10 min in, 20 min in, and immediately following the 30-min activity.

Genetic Analyses: DNA Collection, Extraction, and Storage

DNA from cheek swabs was collected and extracted following published procedures (see Freeman et al., 1997; Hutchison, McGeary, Smolen, Bryan, & Swift, 2002; Walker et al., 1999). The *BDNF* SNP was assayed using a commercially available 5′-nuclease (TaqMan, Roche Molecular Systems, Pleasanton, CA) assay in conjunction with the 7500 thermocycler (Applied Biosystems, Foster City, CA; see Livak, 1999, for description of the TaqMan assay). Several recent studies examined the effects of an SNP (G/A at nucleotide 196; Rs6265) in the *BDNF* gene that results in a valine to methionine substitution (Egan et al., 2003; Hariri et al., 2003). This substitution results in a change in *BDNF* localization and impairment of BDNF secretion that adversely impacts hippocampal function and memory (Egan et al., 2003), demonstrating that this is a functional polymorphism. On the basis of their genotypes, participants were classified into two groups: One group represented the more common genotype (G/G; 63% of sample, $n = 37$), and the second group represented the less frequent genotypes (A/G and A/A; 37% of sample, $n = 22$). Previous studies have suggested that the frequency of the A allele ranges from 18% to 45% across different samples and ethnic groups (e.g., Bian, Zhang, Zhang, & Zhao, 2005; Egan et al., 2003; Hariri et al., 2003).

Results

Overview

Key to our model is the central idea that a bout of aerobic activity induces changes in mood. To confirm that this was the case, we conducted repeated measures analyses of variance (ANOVAs) for the POMS and the PAAS separately. A series of analyses were then conducted to test linkages in our theoretical model; specifically to determine whether (a) a polymorphism of the BDNF is associated with acute responses to exercise in the laboratory, (b) differential exertion and temperature regulation predict differential positive mood response to exercise, (c) both positive mood increases and lower perceived exertion in response to exercise are associated with higher motivation to exercise, and (d) higher motivation is associated with greater exercise behavior. Finally we estimated an exploratory path model simultaneously testing multiple linkages in our conceptual framework.

The first analysis was a 2 (condition: exercise or sedentary activity) × 5 (time: preactivity, 5 min into activity, 10 min into activity, 20 min into activity, postactivity) within-subjects repeated measures multivariate analysis of variance (MANOVA) on our multiple measures of mood taken before, during, and after exercise. These were the PAAS subscales of Positive Affect, Negative Affect, Tranquility, and Fatigue. F tests for both MANOVAs are the Wilks's Lambda F approximation for multivariate tests. For all MANOVA and ANOVA findings we also report eta squared as our measure of effect size, which is equivalent to R^2, in that it describes the percentage of variance in the outcome accounted for by that factor. Cohen's guidelines for small, medium, and large effects as assessed by eta squared are .01, .09, and .25, respectively (Cohen, 1988).

The Mood × Condition × Time interaction was significant, $F(12, 52) = 7.81$, $p < .001$, $\eta^2 = .64$, suggesting that changes in mood over time differed depending on whether the participant was in the sedentary or the exercise condition, allowing us to examine the univariate effects for each measure of mood as protected tests (Stevens, 2002). There was a significant Condition × Time effect for positive affect, $F(4, 252) = 31.95$, $p < .001$, $\eta^2 = .34$. As can be seen in Figure 2, positive affect increased slightly over time, $F(4, 252) = 12.6$, $p < .001$, $\eta^2 = .17$, peaking at immediate postactivity, in the exercise condition, whereas positive affect decreased over time, $F(4, 252) = 29.61$, $p < .001$, $\eta^2 = .32$, in the sedentary condition. There was also a significant Condition × Time effect for tranquility, $F(4, 252) = 6.18$, $p < .001$, $\eta^2 = .09$,

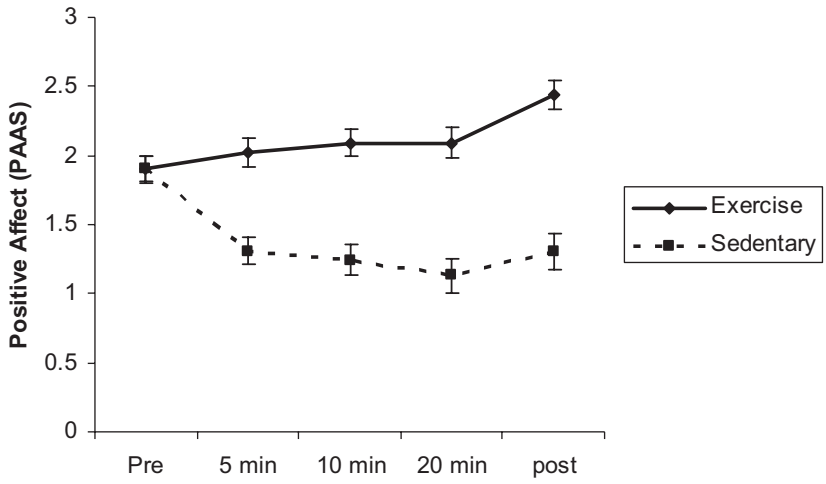

Figure 2. The effects of acute exercise on the Positive Affect subscale of the Physical Activity Affect Scale (PAAS). Positive affect increased in the acute exercise condition but not in the sedentary (control) condition. Pre = preactivity; 5 min = 5 min into the activity; 10 min = 10 min into the activity; 20 min = 20 min into the activity; post = postactivity.

following the same general pattern as positive affect, with an increase in tranquility over time in the exercise condition, $F(4, 252) = 22.29$, $p < .001$, $\eta^2 = .26$, and a significant drop, $F(4, 252) = 5.02$, $p < .001$, $\eta^2 = .07$, in the sedentary condition. A significant Condition × Time effect for fatigue, $F(4, 252) = 4.35$, $p < .01$, $\eta^2 = .06$, showed significantly reduced ratings for fatigue in the exercise condition, $F(4, 252) = 4.40$, $p < .01$, $\eta^2 = .07$, and slightly increased fatigue in the sedentary condition, $F(4, 252) = 9.20$, $p < .01$, $\eta^2 = .13$. There was no Condition × Time interaction for negative affect, $F(4, 252) = 1.97$, $p = .11$, $\eta^2 = .03$.

Because of the length of the POMS, it was administered immediately prior to the activity and immediately after the activity only. An analogous MANOVA was conducted on the POMS subscales of Tension, Depression, Vigor, and Elation, this time in a 2 (condition: exercise or sedentary activity) × 2 (time: preactivity, postactivity) within-subjects repeated measures design. Again the overall Mood × Condition × Time interaction was significant, $F(3, 60) = 24.43$, $p < .001$, $\eta^2 = .55$, allowing us to examine univariate effects. There was a significant Condition × Time interaction for elation, $F(1, 62) = 45.76$, $p < .001$, $\eta^2 = .42$, following the pattern of effects for the Positive Affect subscale of the PAAS. Elation increased from pre to post in the exercise condition, $F(1, 62) = 24.74$, $p < .001$, $\eta^2 = .29$, and decreased over the same period in the sedentary condition, $F(1, 62) = 14.13$, $p < .001$, $\eta^2 = .19$. Similarly, there was a significant Time × Condition interaction on vigor, $F(1, 62) = 76.14$, $p < .001$, $\eta^2 = .55$. Feelings of invigoration increased significantly in the exercise condition, $F(1, 62) = 35.29$, $p < .001$, $\eta^2 = .36$, and decreased significantly in the sedentary condition, $F(1, 62) = 45.37$, $p < .001$, $\eta^2 = .42$. Condition × Time effects on the other POMS subscales were not significant: tension, $F(1, 62) = 1.48$, $p = .23$, $\eta^2 = .02$; depression, $F(1, 62) = 0.03$, $p = .86$, $\eta^2 = .00$. Generally speaking, our data validate a relation between increases in positive affective states (increased positive mood, tranquility, elation, and vigor; decreased exhaustion) and acute exercise behavior, as opposed to with a sedentary control. The key linkage in our model, between exercise and positive mood, is thus established.

Genetic Moderator of the Affective and Physiological Effects of Exercise

A series of 5 (time: preactivity, 5 min into activity, 10 min into activity, 20 min into activity, postactivity) × 2 (BDNF: G/G vs. G/A and A/A) mixed design ANOVAs were run on the significantly affected PAAS subscales of Positive Affect, Fatigue, and Tranquility. Gene was thus a two-level between-subjects factor, whereas time was a within-subjects factor. Analogous ANOVAs were conducted for the Vigor and Elation subscales of the POMS, with the exception that time is only a two-level (preactivity, postactivity) within-subjects variable. In these analyses, we were interested in the moderating influence of the gene on reactions to exercise specifically, so these analyses eliminated the sedentary condition and were conducted only on the exercise session data.

There was a significant BDNF × Time interaction on the Positive Affect, $F(4, 228) = 2.50$, $p < .05$, $\eta^2 = .04$, but not on the Tranquility, $F(4, 228) = 1.04$, $p = .39$, $\eta^2 = .02$, or Fatigue, $F(4, 228) = 1.40$, $p = .13$, $\eta^2 = .02$, subscales of the PAAS. There were also no significant Gene × Time interactions on the Elation, $F(1, 56) = .94$, $p = .34$, $\eta^2 = .02$, or the Vigor, $F(1, 56) = 1.23$, $p = .27$, $\eta^2 = .02$, subscales of the POMS. We examined the pattern of means for the two BDNF groups on the Positive Affect subscale of the PAAS (see Figure 3). Those in the A/G or A/A group showed a more pronounced increase in positive affect in response to exercise compared with those in the G/G group.

Physiological and Psychological Mediators

Theoretically, it is reasonable to assume that any particular genetic effect on mood should be at least partially mediated by some physiological or psychological response of the individual

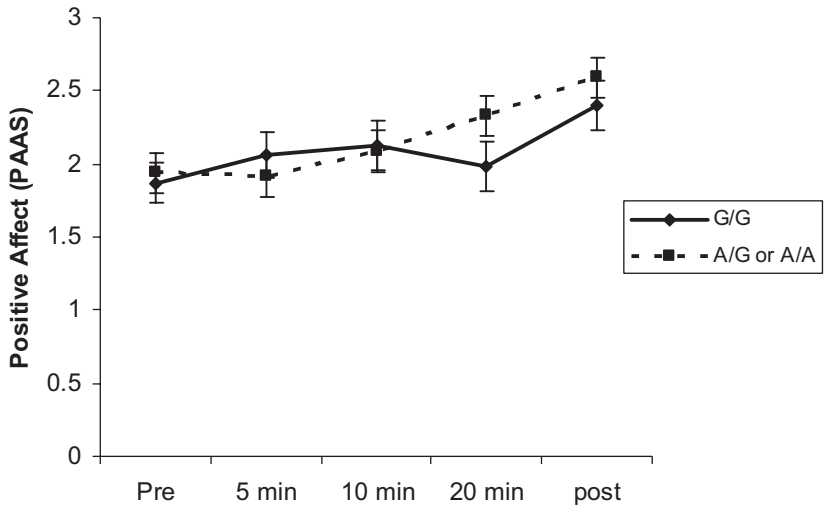

Figure 3. Comparison of Physical Activity Affect Scale (PAAS) Positive Affect subscale scores by brain-derived neurotrophic factor genotype, with the more frequent genotype (G/G) individuals demonstrating significantly lower levels of positive affect during and after exercise compared with lower frequency genotype (G/A and A/A) individuals. Pre = preactivity; 5 min = 5 min into the activity; 10 min = 10 min into the activity; 20 min = 20 min into the activity; post = postactivity.

that is affected by that gene. We looked to perceived exertion, heart rate, and temperature regulation as putative mediators of the BDNF on mood. Ratings of perceived exertion were obtained at the same time points as ratings on the PAAS, so first we conducted the 2 (condition: exercise or sedentary activity) × 5 (time: preactivity, 5 min into activity, 10 min into activity, 20 min into activity, postactivity) repeated measures ANOVA to verify that exercise increased exertion compared with the sedentary condition. Not surprisingly, perceived exertion increased significantly in the exercise condition, $F(4, 252) = 256.00$, $p < .001$, $\eta^2 = .80$, and remained unchanged in the sedentary condition, $F(4, 252) = .47$, $p = .75$, $\eta^2 = .01$. The test of the Time × Condition interaction was significant, $F(4, 252) = 242.69$, $p < .001$, $\eta^2 = .79$. In the next analysis looking for a moderation of changes in exertion during exercise by the *BDNF* SNP, we found a significant Gene × Time interaction, $F(4, 228) = 7.04$, $p < .01$, $\eta^2 = .11$, such that G/G individuals demonstrated greater levels of perceived exertion during exercise (see Figure 4).

Heart rate increased dramatically in the exercise condition, $F(4, 248) = 823.69$, $p < .001$, $\eta^2 = .93$, and decreased significantly,

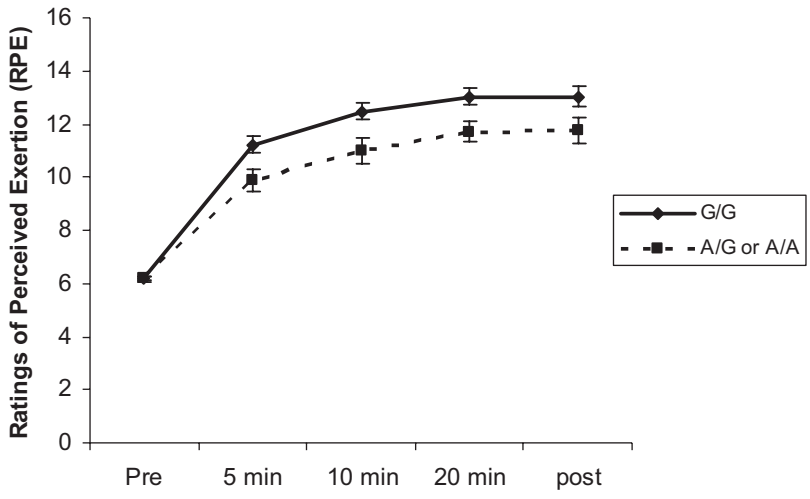

Figure 4. Comparison of Ratings of Perceived Exertion scores by brain-derived neurotrophic factor genotype, with the more frequent genotype (G/G) individuals demonstrating significantly greater levels of perceived exertion during and after exercise compared with lower frequency genotype (G/A and A/A) individuals. Pre = preactivity; 5 min = 5 min into the activity; 10 min = 10 min into the activity; 20 min = 20 min into the activity; post = postactivity.

$F(4, 248) = 31.50$, $p < .001$, $\eta^2 = .34$, in the sedentary condition. The test of the Time × Condition interaction was significant, $F(4, 248) = 847.47$, $p < .001$, $\eta^2 = .93$. As with ratings of perceived exertion, there was also a Gene × Time interaction, such that G/G individuals demonstrated significantly greater heart rate levels during and after exercise, $F(1, 56) = 5.11$, $p < .05$, $\eta^2 = .08$.

There was a significant Condition × Time interaction on temperature, $F(4, 252) = 6.80$, $p < .001$, $\eta^2 = .10$, such that temperature increased significantly in the exercise condition, $F(4, 252) = 3.90$, $p < .01$, $\eta^2 = .06$, and decreased slightly in the sedentary condition, $F(4, 252) = 2.96$, $p < .05$, $\eta^2 = .04$. There was no moderation of change in temperature during the exercise activity by the *BDNF* SNP, $F(4, 228) = .37$, $p = .83$, $\eta^2 = .01$.

Predictors of Exercise Behavior and Motivation to Exercise

Next, we reviewed data more proximal to behavior in the model and examined the relations between mood and both motivation to exercise and exercise behavior. These data are cross-sectional; thus, our assessment of behavior is necessarily a reflection of past exercise behavior. Nevertheless, given the correlation between past behavior and future behavior, and as a first demonstration of our hypothesized model, we utilized the measure of past exercise behavior in these analyses. We hypothesized that an experience of positive mood in response to an acute bout of exercise should be associated with higher motivation to exercise in the future. First, we examined the relations between mood level in response to acute exercise (the value obtained immediately after exercise) and our motivational measures from the TPB (attitudes, norms, self-efficacy, and intentions). As can be seen in Table 1, there were significant relations between self-efficacy and intentions for exercise and PAAS Positive Affect, PAAS Fatigue, POMS Vigor, and POMS Elation in the expected directions. We next conducted an ordinary least squares regression in which we regressed past exercise behavior on attitudes, norms, self-efficacy, and intentions. Both self-efficacy ($B = .32$, $p = .01$, $pr^2 = .10$) and intentions ($B = .33$, $p = .01$, $pr^2 = .11$) were significantly positively associated with actual exercise behavior.

A Preliminary Test of the Model

Ultimately, we would like to estimate multivariate mediational models with latent variables to test some of the hypothesized causal pathways in our model. Given our sample size and cross-sectional limitations in the current study, we tested a simple path model that exemplifies one of the possible pathways in the model. We estimated a path model in EQS 6.1 (Bentler, 2005; see Figure 5). Initial estimation of the model indicated an additional path not originally hypothesized leading directly from ratings of perceived exertion to exercise behavior. Given the cross-sectional nature of the data, this path is more accurately characterized as a reciprocal influence of exercise on perceived exertion, such that individuals who exercise more feel less exertion associated with exercise. With the addition of this path, the fit of the model was adequate, $\chi^2(5, N = 59) = 3.94$, $p = .56$, comparative fit index = 1.00, root-mean-square error of approximation = .00, 90% confidence intervals on the root-mean-square error of approximation = .00, .16, and all hypothesized paths were significant. Standardized path coefficients appear in Figure 5. As can be seen in the figure, G/G individuals experienced higher perceived exertion than did A/A or A/G individuals, and higher perceived exertion was related to less increase in positive mood. More positive mood in response to exercise was related to higher intentions to exercise, and higher intentions were associated with more frequent exercise behavior. Though this preliminary model has all the inherent limitations of cross-sectional data, we believe it provides strong evidence for our conceptualization of a possible pathway whereby genetic differences could influence exercise behavior.

Discussion

The findings of the present study were largely consistent with the model proposed in Figure 1. The analyses indicated that acute physiological responses to exercise and the interpretation of these responses (e.g., perceived exertion) influence the effects of exercise on mood, which in turn relate to intentions and motivation to exercise in the future. Although numerous studies have reported that exercise increases positive mood, the present study provides a more detailed analysis of factors that influence positive mood during and after exercise as well as an analysis of whether these effects are important for intentions and motivation to exercise in the future. For example, the association between increases in positive mood and exercise intentions represents a novel contribution to this area of research. These data support the notion that individuals who experience more positive mood after exercise are also more likely to want to exercise in the future. In addition, these data also support the hypothesis that physiological responses to exercise are significant predictors of positive mood after exercise. Thus, multilevel, transdisciplinary models of exercise behavior may be useful in terms of identifying upstream constructs that influence exercise behavior. Finally, the present study provides a framework for the incorporation of other variables that might play

Table 1
Correlations Among Immediate Postexercise Mood and Exercise Motivation

Motivation variable	PAAS Positive Affect	PAAS Tranquility	PAAS Fatigue	POMS Vigor	POMS Elation
Attitudes	−.15	−.003	.06	−.07	−.24*
Norms	.17	−.12	−.06	.06	.04
Self-efficacy	.36**	−.02	−.25*	.32**	.28*
Intentions	.40***	−.17	−.42***	.24†	.26*

Note. PAAS = Physical Activity Affect Scale; POMS = Profile of Mood States.
† $p < .10$. * $p < .05$. ** $p < .01$. *** $p < .001$.

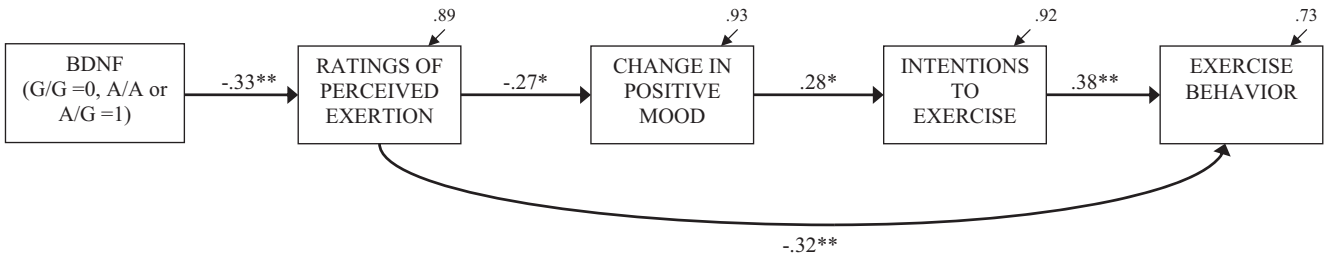

Figure 5. Mediational model of genetic effects, physiological and psychological effects of exercise, and exercise behavior. Overall model fit: $\chi^2(5, N = 59) = 3.94$, $p = .56$, comparative fit index = 1.00, root-mean-square error of approximation (RMSEA) = .00, 90% confidence intervals on the RMSEA (.00, .16), Significance levels for paths: $^{*}p < .05$, $^{**}p < .01$. BNDF = brain-derived neurotrophic factor.

an important role in moderating the proximal or distal effects of exercise.

As proof of concept, in the present study we tested the influence of a functional SNP in a gene that is likely to play an important role in exercise behavior and the beneficial effects of exercise. Preliminary results suggest that the *BDNF* SNP has a small, direct influence on positive mood but strong effects on ratings of perceived exertion and heart rate in response to a bout of aerobic activity. It is important to note that the *BDNF* SNP is only one of many possible genetic factors that may influence acute responses to exercise and future exercise behavior. Larger sample sizes will be needed to test other sources of genetic variation and the additive and interactive effects of different sources of genetic variation (for a review, see Rankinen et al., 2004).

A related problem with our relatively small sample size is that it prevented us from making reliable cross-group distinctions on the basis of gender, race, or age. Another interesting cross-group analysis for future research would be to compare regular exercisers with sedentary individuals to test whether the relation between responses in the laboratory in terms of physiology and mood and measures of exercise motivation and behavior are similar in people who exercise regularly versus those who do not. This is crucial, as ultimately we seek to move sedentary individuals to regular exercise, so it is important to understand physiological and psychological responses to initiating an exercise program. An additional limitation of the present study is our reliance on a cross-sectional measure of behavior, preventing us from making any causal assertions about the relations between responses in the lab, motivation, and exercise behavior. In addition, given the links between exercise and depression and between BDNF and depression, it would have been useful to have included a measure of depression in this study.

Another important issue this study does not address is the exact mechanism of influence of the *BDNF* SNP on physiological responses such as heart rate and perceived exertion in response to exercise. This mechanism—or perhaps mechanisms—is currently not known. TrkB, the receptor for BDNF, appears not to be expressed in the adult heart under normal circumstances (Shibayama & Koizumi, 1996), making it unlikely that BDNF alters heart rate directly. However, TrkB is expressed in a large number of brain structures, including the hypothalamus and other autonomic structures involved in heart rate regulation (Berg-von der Emde et al., 1995), and although effects on several brain structures might account for these effects, one possibility is that BDNF may affect heart rate through a neuromodulatory influence on the autonomic nervous system. Consistent with this hypothesis, injection of BDNF into the rostral ventrolateral medulla increased arterial pressure in anesthetized rats (Wang & Zhou, 2002). However, these authors also found no effect of BDNF on resting heart rate in this model, and intrathecal infusion of several different concentrations of recombinant *BDNF* into conscious dogs also had no effect on resting heart rate (Yaksh et al., 1997). In the present study, participants with the G/G SNP, which is associated with greater BDNF secretion (Egan et al., 2003), showed a greater heart rate response to exercise than did participants with the A/A or A/G genotype. Because preexercise heart rate was not significantly different between participants with different *BDNF* genotypes, our data are consistent with the hypothesis that BDNF levels do not affect resting heart rate but instead modulate the heart rate response to submaximal exercise. Together these data suggest that the role of BDNF on physiological responses, even relatively straightforward ones such as heart rate, is quite complex.

It is interesting to note that there was no reliable direct relationship between the *BDNF* SNP and past exercise behavior. This is an excellent demonstration of the weakness of many genetic designs that seek to find quantitative relationships between a single gene and a complex behavioral outcome (e.g., studies that seek a relationship between one gene, such as *DRD2*, and the complex disease of alcoholism; Noble, 1998). Such studies typically reveal small and inconsistent effects. This situation in behavioral genetic research has led to the suggestion that behavioral scientists should narrow and refine their phenotypes and assure that these narrower phenotypes are plausibly related to the genetic factor of interest (e.g., Leboyer et al., 1998; Schuckit, 1999; Swan, 1999). In essence, the recommendation is that scientists should conceptualize models that include intermediate precursors that are associated with the outcome (in our case, mood responses, motivation, etc.) that may be more proximal to a genetic mechanism (*BDNF*) and also related to the more distal phenotype (exercise behavior; see Hutchison, Stallings, McGeary, & Bryan, 2004).

Despite its limitations, this preliminary study provides an initial framework for the examination of genetic factors that may influence exercise behavior. It also provides a framework for conceptualizing the development of new interventions or tailored interventions. Physical activity intervention research has reached the point at which it is clear that some intervention strategies work better than others. Identifying variables that predict who is likely to respond to different kinds of interventions is critical in increas-

ing the positive impact of these interventions (Baranowski, Anderson, & Carmack, 1998; Bauman, Sallis, Dzewaltowksi, & Owen, 2002). More effective interventions to increase physical activity and decrease the risk for cancer, heart disease, and Type II diabetes are sorely needed, and the successful development of these interventions hinges on a multilevel, transdisciplinary understanding of the biological, psychological, and genetic mechanisms that may moderate the effectiveness of these interventions. In forthcoming work, we will implement a theory-based physical activity intervention (cf. Marcus, Bock, et al., 1998; Marcus, Emmons, et al., 1998; Marcus, Napolitano, & Lewis, 2003) and conduct a thorough and rigorous investigation of the genetic, physiological, and psychological moderators of program effectiveness, guided by the transdisciplinary model initially tested here. In sum, we see this model as a useful framework for the basic study of the genetic, physiological, and psychological processes involved with voluntary exercise, as well as a valuable tool for the applied examination of tailored exercise interventions and their efficacy for different subsets of individuals.

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