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Sensation seeking genes and physical activity in youth

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Abstract

Many studies examining genetic influences on physical activity (PA) have evaluated the impact of single nucleotide polymorphisms (SNPs) related to the development of lifestyle-related chronic diseases, under the hypothesis that they would be associated with PA. However, PA is a multi-determined behavior and associated with a multitude of health consequences. Thus, examining a broader range of candidate genes associated with a boarder range of PA correlates may provide new insights into the genetic underpinnings of PA. In this study we focus on one such correlate – sensation seeking behavior. Participants (N=1,130 Mexican origin youth) provided a saliva sample and data on PA and sensation seeking tendencies in 2008–09. Participants were genotyped for 630 functional and tagging variants in the dopamine, serotonin, and cannabinoid pathways. Overall 30% of participants (males – 37.6%; females – 22.0%) reported ≥60 minutes of PA on five out of seven days. After adjusting for gender, age and population stratification, and applying the Bayesian False Discovery Probability approach for assessing noteworthiness, four gene variants were significantly associated with PA. In a multivariable model, being male, having higher sensation seeking tendencies and at least one copy of the minor allele for SNPs in ACE (rs8066276 OR=1.44; p=0.012) and TPH2 (rs11615016 OR=1.73; p=0.021) were associated with increased likelihood of meeting PA recommendations. Participants with at least one copy of the minor allele for SNPs in SNAP25 (rs363035 OR=0.53; p=0.005) and CNR1 (rs6454672 OR=0.62; p=0.022) have decreased likelihood of meeting PA recommendations. Our findings extend current knowledge of the complex relationship between PA and possible genetic underpinnings.

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Keywords

Physical Activity; Genes; Sensation Seeking; Mexican origin youth

Introduction

The health benefits of engaging in regular moderate physical activity (PA) are well known (Blair & Morris, 2009; Hallal et al. 2006). Although these benefits have been well established, over the last decades, average levels of PA have decreased while time spent in sedentary activities has increased (Nelson *et al.* 2006). PA is a complicated multi-dimensional behavior that is influenced by upstream environmental, psychosocial and physiological factors and involves human movement via musculoskeletal contraction and results in physiological consequences (Pettee Gabriel *et al.* 2012). Evidence suggests that the propensity to engage in PA aggregates in families (Simonen *et al.* 2002), underscoring the possibility that there is a genetic component to engaging in PA. Hereditability estimates based on twin studies range between 0% and 85% depending upon the age of the participants and PA phenotype examined (Strubbe *et al.* 2005), however among family members estimates are lower, ranging between 0% (Perusse *et al.* 1989) and 57% (Butte *et al.*, 2006). In general, among adults, this familial aggregation is largely a function of genetic factors, however in adolescence a combination of genetic and shared environmental factors drive the observed aggregation in families (Strubbe *et al.* 2005; de Moor *et al.* 2011).

In addition to linkage studies (e.g. Cai *et al.* 2006; Simonen *et al.* 2003a) and genome-wide association studies (De Moor *et al.*, 2008; Simonen *et al.* 2003b), many studies examining genetic influences on PA have evaluated the impact of single nucleotide polymorphisms (SNPs) associated with lifestyle-related chronic diseases, under the hypothesis that they also would be associated with PA (Mori *et al.* 2009). However, across the life-course, PA is associated with a decreased risk for many health risk factors and outcomes (Blair & Morris, 2009), including improved cognitive functioning (Davis *et al.* 2011) and mental health (Stathopoulou *et al.* 2006; Mata *et al.* 2011). In youth, PA has been shown to increase as sensation seeking tendencies increase (Sallis *et al.* 2000; Wilkinson *et al.* 2012). Because PA is a multi-determined behavior and associated with a multitude of health consequences, examining polymorphisms associated with these other correlates may provide new insights into the genetic underpinnings of PA behavior. One such correlate is sensation seeking behavior.

Derringer *et al.* (2010) reported that multiple dopamine system genes accounted for significant inter-individual variation in sensation seeking behaviors. In a commentary on the relationship between genes and PA, Knab and Lightfoot (2010) speculated on the potential causal role of genes in the dopamine system. Since the primary neurotransmitter of the reward pathway is dopamine, genes for dopamine synthesis, degradation, receptors, and transporters are reasonable candidates (Knab & Lightfoot, 2010). However, serotonin and cannabinoid neurons modify both dopamine metabolism (Larsen *et al.* 2012; Melis & Pistis, 2007) and neurons, therefore also are considered relevant pathways to include when studying specific aspects of human behavior. Thus, our goal in the current analysis was to examine associations between meeting public health recommendations for PA and genes in the dopamine, serotonin, opioid and cannabiniod pathways, which have been previously associated with sensation seeking tendencies, risk taking behaviors, and health conditions such as Attention Deficit and Hyperactivity Disorder (ADHD) that are also related to sensation seeking or risk taking behaviors (Glass & Flory, 2010). Understanding the roles of both environmental and genetic factors on PA behavior among adolescents has important

ramifications for long-term chronic disease prevention as PA habits established in adolescence tend to track into adulthood (Tammelin *et al.* 2003; Paavola et al. 2004).

Materials and Methods

Design and study participtants

Our data were derived from Mexican origin adolescents who were participants enrolled in a prospective cohort study of smoking behavior that began in 2005–06. In 2008–09, the study aims were expanded to examine the relationship between PA and smoking initiation. Participants were drawn from a population-based cohort of Mexican-American households launched in 2001 by the Department of Epidemiology at The University of Texas M. D. Anderson Cancer Center, called the Mano-a-Mano Mexican American Cohort Study (MACS). To be eligible to participate in the MACS, participants had to self-identify as Mexican or Mexican American; thus all parents of our participants are either Mexican or Mexican American. Households were initially recruited into the cohort from predominantly Mexican American neighborhoods in Houston, Texas using probability random-digit dialing, door-to-door recruitment, intercepts, and networking approaches. Results from these pooled recruitment methods indicated no significant differences in populations by recruitment method with respect to language preference, country of origin, years living in the US, and household income. A detailed description of the cohort recruitment methodology has been published (Wilkinson *et al.* 2005). A total of 3,000 households with potential age-eligible (adolescents between the ages of 11 and 13 years) participants were identified from the cohort database. Of the first 1,425 potential participants' parents or legal guardians contacted to assess interest in the study, just over 90% agreed to enroll their child in the study (N=1,328) at baseline. All parents and legal guardians provided informed consent and all minors provided informed assent. The institutional review board at The University of Texas M. D. Anderson Cancer Center approved all aspects of this study.

Data Collection

The survey data included in the current analysis were collected via personal interview in the home in 2008–09. Informed written consent and saliva samples were obtained at baseline roughly 30 months earlier, when the participants enrolled in the study. Most participants (N=1,154 or 86.9% of those enrolled at baseline) provided data in 2008–09. Participants answered the survey either in English or Spanish on a hand-held personal digital assistant to ensure privacy and received a $25 gift card upon completion of the interview. A detailed description of the data collection procedures has been published (Wilkinson *et al.* 2008).

Survey measures

All participants provided demographic information (gender, age, country of birth) when they enrolled at baseline. Household socio-economic status (SES) was assessed using parental educational attainment rather than household income because more than 40% of the parents did not report their income, while the majority reported educational attainment. Educational attainment was categorized into three levels: "less than high school," "high school/General Educational Development equivalency" or "more than high school."

Physical activity

was assessed using the following two items, both of which were adapted from the Youth Risk Behavioral Surveillance System (YRBSS; 2): "Think about the activities you do at school, but not in PE. On how many days of the past 7 did you exercise or participate in physical activity for at least 60 minutes per day?" and "Think about activities you do in your community or at home. On how many days of the past 7 did you exercise or participate in

physical activity for at least 60 minutes per day?" To be consistent with public health recommendations for PA in youth that were available when the cohort began (2005–06), both variables were used. Participants who reported being physically active for at least 5 days were classified as meeting public health recommendations for PA for adolescents and were coded as "1"; and participants reporting ≤ 5 days were classified as not meeting PA recommendations and coded as "0" (CDC, 2005). PA reported in PE was excluded because fewer than 10% of schools nationwide require PE on a daily basis (Lee *et al.*, 2006) and the length of time engaging in higher intensity PA while in PE is limited (Fairclough & Stratton, 2005).

Sensation seeking

tendencies were assessed using 12-items from the Thrill and Adventure Seeking (TAS) subscale on the Sensation Seeking Scale for Children (SSSC; Russo *et al.* 1993). Participants select the response that most describes what they like or feel, for example "a) I'd never do anything that's dangerous" or "b) Sometimes I like to do things that are a little scary." The scale demonstrates good internal reliability (TAS; alpha=0.81) based on data from the participants. We created a three-level variable with equal numbers per level, based on the distribution of the TAS because the variable was skewed toward high TAS. Thus, participants with a score of five or less were classified as having "low" levels of TAS, those with a score of six, seven, or eight were classified as having "medium" levels of TAS and those with a score of nine or more were classified as having "high" levels of TAS.

Subjective Social Status

the adolescent's subjective view of where he or she lies in the school-based social hierarchy, was assessed using a version of the MacArthur Scale of Subjective Social Status adapted for adolescents (Goodman *et al.* 2001). This 10-point scale is constructed in the shape of a ladder with the following descriptions and instructions. "At the top of the ladder are kids who are the best off – get good grades, have lots of friends, or do well at sports. At the bottom, are kids who are worst off – get poor grades, have few friends, or do poorly in sports. Choose the one rung where you think you are on the ladder." We created a three-level variable with equal numbers per level, based on the distribution of subjective social status because the variable was skewed toward high subjective social status. Thus, participants with a score of seven or less were classified as having "low" subjective social status, those with a score of eight were classified as having "medium" subjective social status and those with a score of nine or ten were classified as having "high" subjective social status.

DNA collection

Saliva samples were obtained in Oragene vials (DNA Genotek, Ottawa, Ontario, Canada). DNA extraction was performed using a ''Purifier'' solution with alcohol precipitation per the manufacturer's protool. The median yield of DNA from 2 mL of saliva captured in 2 mL of Oragene•DNA was 110 μg.

SNP selection and Genotyping

Candidate genes were identified from published reviews (Kreek *et al.* 2004) and pub-med searches using the following key words: sensation seeking, novelty seeking, risk taking, gambling, smoking, and alcohol use. This list was cross-referenced with the Gene Ontology Database (http://pid.nci.nih.gov/) and Kegg Pathway to confirm pathway information. Tagging SNPs were selected from the International HapMap Project (Release 21 with NCBI build 36; http://www.hapmap.org). The following selection criteria were used: located in the respective gene or within 10 kb upstream or downstream of the gene ends to cover the

regulatory regions; minor allele frequency (MAF) >5% in various ethnic groups; and not already represented by a current tag SNP at a linkage disequilibrium (LD) of r^2>0.80. We also included SNPs in coding (synonymous SNPs, nonsynonymous SNPs) and regulatory regions (promoter, splicing site, 5-UTR, and 3-UTR). Genotyping was conducted following standard procedures, which are described in detail elsewhere (Wilkinson *et al.* 2012).

Statistical analyses

Chi-square tests were used to compare socio-demographic characteristics and categorical measures of TAS and subjective social status, as well as genotypes by meeting vs. not meeting PA recommendations. Linkage disequilibrium (LD) between SNPs was assessed by calculating pairwise Lewontin's D' and r^2 using Haploview version 3.32.

SNPs were selected for inclusion in the multivariable models using Bayesian False Discovery Probability tests (BFDP; Wakefield, 2007) to evaluate the chance of false positive associations for the variants studied. We set four levels of prior probability (0.01, 0.03, 0.05, and 0.07), prior odds ratio (OR) at 1.5, and the selected level of noteworthiness for BFDP at 0.8, the recommended threshold by Wakefield (2007). This process resulted in the identification of 10 significant SNPs. Next, because a priori we do not know the mode of inheritance, we tested each significant SNP using dominant, recessive, and additive models and selected the most parsimonious. The dominant model was the most parsimonious model for all 10 SNPs identified using BFDP tests. All 10 SNPs were entered simultaneously into an unconditional logistic model controlling for gender and age using a backward stepwise selection criteria.

Principal components analysis was conducted to test for the possible underlying ethnic stratification, with the use of EIGENSTRAT software (Price *et al.* 2006). We applied the principal components analysis to the genotype data to infer continuous axes of genetic variation, which are defined as eigenvectors. Finally, a multivariable unconditional logistic regression model was fit including the psychosocial variables that demonstrated an association with PA of $p \leq 0.2$, the four gene variants that were significantly associated with PA from the SNP selection process, and the top two axes of variation from the principal components analysis. All were simultaneously entered into the model. In addition, because many researchers report a strong association between age and PA in youth (e.g. Belcher *et al.* 2010; Wall *et al.* 2011), child's age was included in the model regardless of the strength of the association found between participant age and PA.

Results

Of the 1,274 youth enrolled at baseline for who DNA was available, 1,132 provided PA data in 2008–09. Two participants were missing data on subjective social status. Thus the sample size for the current analysis was 1,130; 572 (50.6%) were female. Overall 29.7% of participants reported that they accumulated sufficient PA to meet recommendations (Table 1). Significantly more males than females were physically active (chi-square=32.93; df=1; p<0.001). Meeting PA recommendations was not associated with the child's age, country of birth, BMI, or with parental educational attainment. Although there were no significant differences in level of subjective social status by level of PA, 26.0% of those with low subjective social status reported not meeting PA recommendations compared with 32.2% of those with high subjective social status. Participants who met PA recommendations reported higher mean levels of sensation seeking tendencies on the TAS subscale and a larger proportion of those classified as having high levels of TAS reported meeting PA recommendations compared to their peers with lower levels (chi-square=22.93; df=2; p<0.001).

Genotyping was completed on a total of 630 SNPs; 8 SNPs had missing genotype data for all participants, 12 SNPs failed the Hardy Weinberg Equilibrium Test ($p<0.00001$) for the entire data set, and an additional 36 SNPs were removed because minor alleles frequencies were too small to draw valid inference. Thus 574 SNPs were included in the analysis. There were 43 SNPs with $p<0.05$ based on the best model fit (additive, dominant, or recessive model). After controlling for false discovery, we identified ten SNPs with a statistically significant BFDP at 0.8 and prior probability of 0.05. Using unconditional logistic regression analysis with backward selection and adjusting for participants' gender and age, four of the ten SNPs were selected at $p\leq0.05$. Table 2 presents the distribution of the four SNPs retained for the multivariable analyses (two in the dopamine pathway (rs363035 and rs8066276), one in the serotonin pathway (rs11615016), and a cannabiniod receptor variant (rs6454672), while Table 3 presents more detailed information on each SNP. The gene, position, allelic change and chromosome location for all the SNPs are presented in supplementary table 1.

To conduct the principal components analysis, we used N=1,132 participants and 531 SNPs, which were shown to be unassociated with PA outcome at a significance level 0.05 based on the best model fit (additive, dominant, or recessive model). Here we used the quality control criteria of MAF > 5% and Hardy-Weinberg equilibrium p value > 10^{-5} in controls (i.e. adolescents not meeting public health recommendations for PA). We did not observe significant ethnic stratification in our data from the principal components analysis. Because only the top 2 eigenvalues (derived from the top 2 principal components) were significantly larger than the subsequent eigenvalues, we used these 2 largest principal components in our analyses (Nassir *et al.* 2009; Tian *et al.* 2008). We also considered controlling for the top 3, 5 and 10 largest principal components but found no significant differences in the results of association between SNPs and PA.

Table 4 presents the results from the multivariate model including the psychosocial and genetic data. Of all the covariates we examined, gender maintained the strongest association with meeting PA recommendations (OR=1.96; 95% CI: 1.48–2.95; $p<0.001$). Higher levels of both thrill and adventure seeking (OR=1.29; 95% CI: 1.09–1.53; p=0.003) and subjective social status (OR=1.27; 95% CI: 1.08–1.50; p=0.003) were associated with meeting PA recommendations. All four SNPs we examined also maintained a significant association with PA. The minor alleles of the SNPs we identified in tryptophan hydroxylase 2 gene (TPH2; OR=1.73; 95% CI: 1.09–2.75; p=0.021) and in angiotensin I converting enzyme gene (ACE; OR=1.44; 95% CI: 1.08–1.91; p=0.012) were associated with increased likelihood of meeting PA recommendations, while those of the SNPs we identified in synaptosomal-associated protein 25 gene (SNAP25; OR=0.53; 95% CI: 0.34–0.83; p=0.005) and in the cannabinoid receptor 1 gene (CNR1; OR=0.62; 95% CI: 0.41–0.93; p=0.022) were associated with decreased likelihood of meeting PA recommendations. For each of the genetic variants, the odds ratio is associated with the presence of the minor allele (dominant genetic model) referred to in Table 2.

Discussion

In this sample of Mexican origin youth, after adjusting for age and SES, we found gender, TAS tendencies, subjective social status, and four of the ten SNPs significant in univariate analysis were associated with meeting PA recommendations. Two of the SNPs (ACE and SNAP25) were on the dopamine pathway, one was a cannabinoid receptor (CRN1) and the other was TPH2, a serotonin receptor.

Consistent with previous research among Hispanic children and adolescents, we found a higher proportion of males met PA guidelines (Wright, 2011). Also consistent with previous

research, we found that higher levels of sensation seeking tendencies were associated with meeting PA recommendations (Salis *at al.* 2001; Wilkinson *et al.* 2012). While the impact of subjective social status has been examined in relation to smoking (Wilkinson *et al.* 2009), alcohol (Wilkinson *et al.* 2011) and obesity (Goodman *et al.* 2001) to the best of our knowledge this is the first study to report a positive relationship between subjective social status and participation in PA. However, our findings are consistent with previous research examining social reasons why youth participate in sport (Jago *et al.* 2009). Among primary school boys, playing sports is directly related to higher levels of social status; the relationship among girls is more complicated and not as strong (Jago *et al.* 2009).

Many studies report a positive association between PA and SES among youth (e.g. Singh *et al.* 2008), however, we did not observe such an association. In studies that do observe this association, participants represent the full range of SES. Conversely, the participants in our study were from predominantly low income neighborhoods in Houston; just over 80% of the participants parents have a high school education or less. Thus it is possible that we did not observe an association between the two variables because of the restricted range of SES among our participants.

Studies that report a negative association between PA and increasing age include participants with a broader range of age (i.e. from 6 to 19 years) than those in our study (Belcher *et al.* 2010; Bradley *et al.* 2011; Wall *et al.* 2011), and therefore include the age range when the age related decline in PA is most notable. It is possible that we did not observe an association between age and PA because our participants were between 13 and 16 years of age and have already experienced the decrease in PA that is typically observed from middle childhood through late adolescence (Bradley *et al.* 2011).

In addition, we did not find a significant relationship between BMI and meeting PA recommendations among our sample of Mexican origin adolescents, as others have reported (Forshee *et al.* 2004; Kimm *et al.* 2005). We and others have previously observed similar findings (Anderson *et al.* 2009; Strong *et al.* 2011), including greater PA in overweight relative to normal weight Hispanic girls (Byrd-Williams *et al.* 2007). The lack of a consistent relationship may reflect limitations of the self-report PA measures, the importance of energy intake, rather than energy expenditure, to BMI, and/or the limitations of BMI as a measure of adiposity in adolescents (Strong *et al.* 2011).

To date, and to the best of our knowledge, there have been no previous reports of an association between PA and three of the four SNPs that maintained significance in our multivariable model (see review by de Vilhena e Santos *et al.* 2012 and results from a GWA by de Moor *et al.* 2008). ACE, was the first specific gene variant reported to be associated with human performance (Puthucheary *et al.* 2011). In a recent review, ACE insertion/deletion (I/D) polymorphisms have been associated with improvements in physical performance and exercise duration in some populations. Specifically this association has been shown among elite athletes, not amateurs (Puthucheary *et al.* 2011), leading the authors to conclude that the ACE genotype is an important, but single factor, in the determination of an athletic phenotype. Of note, the ACE I/D polymorphism is related to PA performance potentially through its influence on cardiac muscle, skeletal muscle, and oxygen consumption (Puthuchereary et al. 2011) and not through the dopamine pathway. In contrast, the ACE SNP we found associated with meeting PA recommendations in this study has previously been associated with positive coping styles (Heck *et al.* 2008) while PA itself has been linked to improved psychological wellbeing Stathopoulou *et al.* 2006; Mata *et al.* 2011) as well as a decreased use of negative coping strategies such as substance use (Smits *et al.* 2011). These two SNPs, the ACE I/D polymorphism and the SNP we found (rs8066276) are not in LD (please see Figure 1 in Heck *et al.* 2008).

Two of the SNPs (one from SNAP25 and the other from CNR1) are in genes associated with ADHD (Zhang *et al.* 2011; Lu *et al.* 2008) a condition characterized by developmentally inappropriate levels of over-activity or excessive motor activity, inattention, and impulsivity. To the best of our knowledge, while there are no reports of a direct relationship between PA and ADHD, there are reports of the therapeutic benefits of PA on ADHD (e.g. Halpein *et al.* 2012; Field, 2012). Field (2012) suggests that in part these benefits may stem from the release of neurotransmitters such as serotonin and dopamine following different forms of exercise (Strüder *et al.*, 1997). The SNAP complex mediates presynaptic vesicle trafficking and participates in the release of dopamine and other neurotransmitters, such as norepinephrine and serotonin. CNR1 encodes type 1 cannabinoid receptors (CB1), which are mainly located in the central and peripheral neurons where they mediate inhibition of neurotransmitter release, including dopamine. These two genes, previously reported to confer risk for ADHD, were associated with lower odds of meeting PA recommendations in our analysis.

The fourth SNP is from TPH2, an enzyme critical for, and the rate-limiting enzyme in, the synthesis of serotonin (Walther *et al.* 2003). The SNP we identified on TPH2 (rs11615016) is in strong LD (r^2=0.79) with a SNP (rs6582078) reported by Juhasz and colleagues (2010) to be associated with gambling behavior. However, there is no association between this SNP and the aspect of sensation seeking (p=0.08) we examined (data not shown). Furthermore, none of the three other SNPs were associated with this aspect of sensation seeking (p>0.40; data not shown), demonstrating TAS does not mediate the association of these SNPs with PA. However all four SNPs are responsible for neural processing and/or have metabolic functions too, which underscores the possibility that the development of PA habits is associated with alterations in neurotransmitter and metabolic function.

The current study has several strengths. The participants were from a population-based cohort and included roughly equal numbers of girls and boys. In addition, all covariates were assessed using validated measures, and the data were collected in the participants' homes using PDAs, which enabled the participants to read the questions themselves and answer without their parents hearing or viewing their responses, thereby ensuring their privacy. The high retention rate over 30 months—87% of the youth provided data at both contacts—is strength of this study. A final strength of the study is the participants, who represent a large ethnically homogenous and predominantly low-income sample of Mexican origin youth, an understudied population. The households in the population-based cohort from which our participants are drawn are representative of the Mexican origin population in Houston, TX.

Conversely, the main limitation of this study is the lack of an independent replication sample, which is fairly common among minority populations; thus we must consider our finding preliminary. A second limitation pertains to the principle component analysis: without the full set of genome data or Ancestry Informative Markers, the principle component analysis might not be able to identify moderate stratification (Freedman *et al*, 2004; Hao *et al*, 2004; Zou *et al*, 2010). In this study, we conducted a principal components analysis using the unassociated 531 SNPs from all the genes that are available in this study. By using the limited data available, we expected to identify region- or local-specific population structure and adjust for it in the association analysis (Redden *et al.* 2006). Thirdly participants were all of Mexican origin, and therefore the results may not generalize to youth from other ethnic backgrounds, including Hispanics from different countries of origin. A fourth limitation stems from the fact that because we focus on genes in the dopamine, serotonin, opioid, and cannabiniod pathways, we did not examine the role of MC4R, which has previously been linked to energy expenditure and food intake and Hispanic youth (Cai *et al.* 2006). Further, the PA data were self-reported; therefore, derived estimates may be

subject to recall bias. This limitation notwithstanding, unlike many previous studies of children, these data were obtained from the participants, using items adapted from the 2005 YRBSS, and not from a parent/guardian proxy (Bender *et al.* 2005). In addition, we do not know the PA habits of other family members, which could be an important predictor of PA behavior in our participants. Finally, the data are cross-sectional; therefore we can simply examine associations between the constructs of interest – be they genetic or psychosocial – and cannot establish directionality or causality. With regards to the genes we identified, this may mean that the genes have no functional significance.

In conclusion, in the current study we report on four SNPs associated with meeting PA recommendations. Our results confirm previous findings and extend our knowledge of the complex relationship between PA and possible genetic underpinnings. One of the SNPs is located on ACE, a gene previously associated with PA, but among professional-level athletes only. Of the three other SNPs, one on TPH2, is in strong LD with another SNP on TPH2 associated with gambling behavior, while the SNP we identified on SNAP25 is in moderate LD with a SNP on the same gene we find associated with smoking behavior (Wilkinson *et al.* 2012). While our results underscore a potential role for sensation seeking tendencies in the development of PA habits, all four SNPs we identified as associated with PA have clear neural processing and/or have metabolic functions. Additional research is necessary to gain a better understanding of genetic factors associated with the development of PA habits in general and to determine the role of sensation seeking tendencies in the development of PA habits specifically.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Distribution of participant characteristics, subjective social status, and sensation seeking tendencies by level of physical activity (N=1,130)

	Physically Active for at least 60 minutes on at least five out of seven days		
	Yes	No	
	N (%)	N (%)	p-value
Overall	336 (29.7)	794 (70.3)	
Gender			< 0.001
Male	210 (37.6)	348 (62.4)	
Female	126 (22.0)	446 (78.0)	
Age at Follow-up (years)			0.801
12	5 (33.3)	10 (66.7)	
13	78 (30.4)	179 (69.6)	
14	112 (30.4)	257 (69.6)	
15	94 (28.3)	238 (71.7)	
16	45 (31.5)	98 (69.5)	
17	2 (14.3)	12 (85.7)	
Mean (SD)	14.30 (1.04)	14.34 (1.04)	
Country of Birth			0.365
Mexico	94 (32.1)	199 (67.9)	
USA	243 (29.0)	594 (71.0)	
Parental Educational (N=1065)			0.301
< HS	193 (27.6)	506 (72.4)	
HS	55 (30.9)	123 (69.1)	
> HS	62 (33.0)	126 (67.0)	
Body Mass Index			0.747
Mean (SD)	24.98 (6.07)	25.11 (6.43)	
Range	15.35–58.00	14.57–53.63	
Subjective Social Status			0.076
Low	109 (26.0)	311 (74.0)	
Med	106 (30.6)	240 (69.4)	
High	121 (32.2)	243 (66.8)	
Mean (SD)	7.85 (1.48)	7.71 (1.48)	
Range	1–10	1–10	
Thrill & Adventure Seeking			<0.001
Low	86 (22.1)	303 (77.9)	
Med	96 (29.0)	235 (71.0)	
High	154 (37.6)	256 (62.4)	
Mean (SD)	7.64 (3.27)	6.53 (3.25)	
Range	1–12	1–12	

Table 2

Distribution of genes by level of physical activity (N=1,130)

Genes	Minor allele	M*		Physically Active for at least 60 minutes on at least five out of seven days			HapMap minor allele	MATCh minor allele
				Yes	No			
			N (%)	N (%)	N (%)	p-value	%	%
			1,130 (100.0)	336 (29.7)	794 (70.3)			
SNAP25 (rs363035)	A	D					7.0	6.6
GG			986 (87.3)	308 (31.2)	678 (68.8)			
AA/AG			144 (12.7)	28 (19.4)	116 (80.6)	0.004		
CNR1 (rs6454672)	G	D					11.6	8.1
AA			960 (85.0)	300 (31.3)	660 (68.8)			
GG/AG			170 (15.0)	36 (21.2)	134 (78.8)	0.004		
TPH2 (rs11615016)	G	D					3.0	3.9
AA			1043 (92.3)	299 (28.7)	744 (71.3)			
AG			87 (7.7)	37 (42.5)	50 (57.5)	0.007		
ACE (rs8066276)	G	D					48.0	39.5
AA			421 (37.3)	103 (24.5)	318 (75.5)			
AG/GG			709 (62.7)	233 (32.9)	476 (67.1)	0.003		

NB: M = Model; D = Dominant

Table 3

Position, allelic change, physical position and location of each gene (SNP) retained in final model

Gene (SNP)	Position	Allelic Δ	Chr.	Physical Position	Location
SNAP25 (rs363035)	INTRON	C/T	20	10199343–10288079	20p12-p11.2
CNR1 (rs6454672)	INTRON	C/T	6	88876706–88849578	6q14-q15
TPH2 (rs11615016)	5’ UTR	A/G	12	72332626–73059519	12q21.1
ACE (rs8066276)	INTRON	C/T	17	6554423–61599217	17q23.3

Table 4

Logistic Regression for Level of Physical Activity (N=1130)

	OR	95% CI	p-value
Demographic & psychological factors			
Gender (female)	1.96	1.48 – 2.95	<0.001
Thrill & Adventure Seeking (low)	1.29	1.09 – 1.53	0.003
Subjective Social Status (low)	1.27	1.08 – 1.50	0.003
Gene (SNP)			
SNAP25 (rs363035)	0.53	0.34 – 0.83	0.005
CNR1 (rs6454672)	0.62	0.41 – 0.93	0.022
TPH2 (rs11615016)	1.73	1.09 – 2.75	0.021
ACE (rs8066276)	1.44	1.08 – 1.91	0.012

NB: Controlled for child's age and population admixture.