**Defining physical activity trajectories from childhood to young adulthood and characterizing associations with eating disorder risk**

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**Introduction**

**DEx is a concerning, understudied symptom of eating disorders**

Eating disorders are devastating and pernicious psychiatric illnesses, with elevated rates of morbidity,1,2 mortality,1,2 and suicidality.3 One serious, concerning, and understudied feature of eating disorders is dysregulation in physical activity (i.e., driven exercise; DEx). DEx marks increased risk for suicidal behavior,4 poor treatment outcome,5 and eating disorder relapse,6 and specific interventions to target this symptom are lacking.7,8 Despite the relatively high prevalence of DEx in eating disorders (e.g., between 20%-80% of individuals with anorexia nervosa [AN], bulimia nervosa [BN], and other specified eating disorders [OSFED], and about half of treatment-seeking youth with transdiagnostic eating disorders 5,9–11), we know little about the etiology of this behavior.

**Significant, biologically-driven** **variability in physical activity engagement is apparent**

Substantial differences exist in individuals’ experiences of physical activity, including the degree to which one finds physical activity reinforcing and engages in exercise over time.51-52,53. Physical activity levels in the general population are also heritable,12,13 suggesting individual differences in the degree to which physical activity is reinforcing via biobehavioral pathways. Further, a recent genome-wide association study of AN has shown a positive genetic correlation with accelerometer-measured physical activity, suggesting that some of the same factors that increase risk for AN are also operative in determining general physical activity level.14 In terms of biological mechanisms, basic animal and human research indicates that physical activity can engage neurochemical pathways related to both reward promotion,15,16 and threat reduction.17–20 For some individuals, engagement of biological mechanisms, coupled with psychological factors that reinforce exercise, may lead to physical activity patterns that are habitual and compulsive (i.e., DEx).21–30

**Enhanced understanding of the etiology of DEx is critical**

At present, we know relatively little about the etiology of DEx, its relationship to premorbid activity levels, or whether certain patterns of physical activity are associated with risk for DEx and EDs during development. Phenotypic examination of physical activity trajectories across development in relation to DEx and ED risk will be a key step in understanding DEx risk. To date, no research has examined physical activity levels as a *prospective* risk factor for DEx or ED onset. Adult ED patients with DEx retrospectively report being more physically active as children than those without DEx,(Davis et al., 1997) and evaluation of physical activity patters in an epidemiological sample will aid in determining whether very high levels of or changes in physical activity patterns associate with DEx and ED risk. If certain physical activity trajectories associate with higher risk for DEx and/or EDs, this may indicate that vigilance for increased activity patterns could aid in early risk identification.

**Current Study**

The present study aims to characterize physical activity patterns and their associations with DEx and eating disorder risk in a large, epidemiological sample, with followed from late childhood through early adulthood. We will characterize physical activity trajectories and determine if these trajectories associate with a) the symptom of DEx and b) odds of other eating disorder symptoms and eating disorder diagnoses over time. We hypothesize that Several physical activity trajectories will emerge (e.g., stable low, stable high, increasing during adolescence). Further, we expect that trajectories involving high levels of physical activity in late childhood through early adolescence will associate with both DEx and ED risk in adolescence.

**Method**

**Participants**

The present study includes participants from The Avon Longitudinal Study of Parents and Children (ALSPAC). ALSPAC is an epidemiological, longitudinal study of mothers and their children 31–33 Women who were expecting to deliver a child between 1st April 1991 and 31st December 1992 in Avon, UK were invited to take part in the study. Interested expectant mothers provided informed and written consent. Children (*n* = 14,062) from 14,451 pregnancies were enrolled; at one year, 13,988 children were alive. At seven years, 713 additional children were enrolled in the cohort31. The study website contains details of all the data that is available through a fully searchable data dictionary and variable search tool: http://www.bris.ac.uk/alspac/researchers/our-data/. Ethical approval for this study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. Detailed phenotypic, exposure, and socio-demographic data were collected via self- and maternal-report, face-to-face assessments31. Data to be used in the current analyses is outlined below:

**Measures**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Table 1. Assessment time points for PA and ED symptoms with N assessed** | | | | | | | |
| **Age (Years)** | **11** | **13** | **14** | **15** | **16** | **18** | **24** |
| EDs and DEx |  |  | 6213 |  | 5126 | 3372 | 4345 |
| Accelerometer | 6108 | 4783 |  | 2948 |  |  | 2237 |

**Eating Disorder Behaviors**

ED behaviors were self-reported and were measured at 14, 16, 18, and 24 years of age. For each ED behavior, questions inquired about the previous year and were adapted from the Youth Risk Behavior Surveillance System (YRBSS) questionnaire34 which were validated in an epidemiological study of youth35.

*Binge Eating*. Binge eating was defined as eating an unusually large amount of food and feeling out of control during these episodes. Binge eating will be defined as ‘present’ at any time point in which an individual reports binge eating at least once per month.

*Purging*. Purging was defined as making oneself sick or using laxatives to lose weight or avoid gaining weight. Purging will be defined as ‘present’ at any time point in which an individual reports laxative use and/or vomiting at least once per month.

*Fasting.* Fasting was assessed with the question “During the past year, how often did you fast (not eat for at least a day) to lose weight or avoid gaining weight?” with endorsement of at least once per month coded as ‘present’.

*Driven Exercise (DEx).* At age 14, DEx was assessed by the following questions: 1. During the past year, how often did you exercise? 2. Was it difficult for you to do your work or school work because of the amount of time you were exercising? 3. Did you exercise to lose weight or avoid gaining weight? At ages 16, and 18, individuals were also asked if they felt guilty after missing an exercise session? At age 24, exercise was assessed by the following questions: Did you exercise to lose weight or avoid gaining weight even when you were sick or injured? Was it difficult for you to do your work or daily chores/routine because of the amount of time that you were exercising to lose weight or avoid gaining weight?

In line with previous ALSPAC studies,36–38 we will define DEx as ‘present’ for those reporting exercise to manage weight **and** a) feeling guilty after missing exercise sessions b) exercise interfering with work or school or c) exercising even when sick or injured.

**Eating Disorder Diagnoses.**

Eating disorder diagnoses (AN, BN, BED, and purging disorder [PD]) were derived using questionnaire data from the YRBSS from adolescents using DSM-5 diagnostic criteria37,39 . Body mass index (BMI) was an objective measure collected at face-to-face assessment (median ages 13.8, 15.5, 17.8, and 24.0 years) and was included as a diagnostic criterion for AN. Underweight was determined using age, gender, and BMI-specific cutoffs (based on UK reference data);40 corresponding to World Health Organization (WHO) grade 1 thinness.

Parental report of AN symptoms was also used at ages 14 and 16 when formulating AN diagnoses as prior research has shown that parental report often aids in the diagnosis of AN in adolescents due to under-reporting of AN symptoms41. In addition to threshold eating disorder diagnoses, we also identified youth with disordered eating cognitions and behaviors. This category included individuals who reported monthly binge eating, purging excessive exercise, or fasting, along with those who reported more sporadic disordered eating behaviors along with shape and weight concern at age 14, and those who reported eating disorder behaviors at any subthreshold level of severity at ages 16, 18, and 24 years.

**Physical Activity**.

the current study, we will use accelerometer-assessed moderate-to-vigorous physical activity (MVPA) to estimate physical activity trajectories.

**F11 (age 11.5)** ACTIGRAPH SESSION

The ActiGraph™ is a commonly used accelerometer in child and adolescent free-living physical activity studies. At the F11+ clinic, children were asked to wear an MTI Actigraph AM7164 2.2 accelerometer on their right hip for 7 days, beginning the morning after the clinic (Mattocks *et*. *al*., 2008). Summary variables are included in the released dataset. Reinvites have been excluded. Daily variables are not included in the released data as they unlikely to be used in analyses. However, those interested in recoding the raw data are invited to contact ALSPAC.

In addition to the direct measures, there are a number of derived variables that may be useful for analysis:

**CPM**

Total physical activity is the total volume activity including activities at all intensities, measured as the average counts per minute (cpm) over the period of valid recording. This variable is commonly used as it is the summary measure of total physical activity that has been validated against doubly labelled water (*ibid.*). Associations with total physical activity are usually calculated per 100 cpm as this difference is of a similar order to the differences observed between males and females in these data.

**MVPA**

MVPA is the average minutes of moderate to vigorous physical activity per valid day. This variable is commonly used as current physical activity recommendations for children are framed in terms of time spent each day in MVPA. A value of >= 3600 cpm was originally used to define MVPA at the time of the data collection (*ibid*.). More recently, following Evenson *et*. *al*. (2008), who calculated a lower cutpoint of >=2296. Both sets of data are included, where *feag100* - *feag168* use a cut point of =>3600 and *feag200*- *feag238* use a cut-point of >=2296.

**Valid days**

At the time of writing, the definition of a valid day of wear is generally between 480 to 600 minutes. There are two marker variables in the dataset: *feag163* and *feag213*. *feag163* equals 1 when valid data is determined as at least 10 hours (600mins) of valid wear for at least 3 days. This threshold defines a valid day in variables *feag100* - *feag168. feag213* summarises the number of valid days worn overall, based on 500 minutes of wear per valid day. This threshold defines a valid day in variables *feag200* - feag238.

The data contains 140 continuous variables measuring physical activity. Please note that the derivations using different cutpoints and valid day thresholds are clearly defined by the variable labels using the prefix DV: >=3600 or DV: >=2296.

Evenson KR, Cattellier D, Gill K, Ondrak K, McMurray RG. (2008) ‘Calibration of two objective measures of physical activity for children’. *Journal of Sports Science*. (26):1557–65.

Mattocks, C., Ness, A., Leary, S., Tilling, K., Blair, S.N., Shield, J., Deere, K., Saunders, J., Kirkby, J., Smith, G.D., Wells, J., Wareham, N., Reilly, John J. and Riddoch, C. (2008). ‘Use of accelerometers in a large field-based study of children: protocols, design issues and effects on precision’. *Journal of Physical Activity and Health,* 5 (1): S94-S107: https://doi.org/10.1123/jpah.5.s1.s98

**TF2 (Age 13.5)** . The food and movement session describes data collected from the participants over a number of days at home. Two methods of data collection, taken at different times, were used to collect food and movement data.

During clinic, participants were asked to wear activity monitors (accelerometers) to measure movement beginning the day after the clinic visit. The accelerometer, worn on the right hip around the waist, was the Computer Science and Applications (CSA) Inc. ActiGraphTM, model numbers 7164 and 71256. As such, the terms CSA, actigraph and accelerometer are referred to interchangeably in the TF2 meta-data and information sheets.

Three day diet diaries were sent out before clinic to be completed by the adolescent, with parental assistance as needed. Adolescents were instructed to record all food and beverages consumed using standard household measures for the three days, including one weekend day. In order to add precision to the dietary diary data, questionnaires queried for additional information on vitamin supplements, medicine, types of spreads and other foods that were commonly eaten. Participants were asked to bring their completed diaries and food questionnaire with them to clinic.

The CSA ActiGraph™ is a commonly used accelerometer in child and adolescent free-living physical activity studies. At the TF2 clinic, young people were asked to wear the CSA ActiGraphTM accelerometer (model numbers 7164 (serial numbers 10706-27702) and 71256 (serial numbers 51103-52173)) on their right hip for 7 days, beginning the day after clinic attendance. Summary variables are included in the dataset. Reinvites have been excluded.

Below details the derived variables in the dataset that may be useful for analysis. Those interested in recoding the raw data are invited to contact ALSPAC.

**CPM**

Total physical activity is the total volume activity including activities at all intensities, measured as the average counts per minute (cpm) over the period of valid recording. This variable is used as it is the summary measure of total physical activity that has been validated against doubly labelled water. Associations with total physical activity are usually calculated per 100 cpm as this difference is of a similar order to the differences observed between males and females in these data.

**MVPA**

MVPA is the average minutes of moderate to vigorous physical activity per valid day. This variable is commonly used as current physical activity recommendations for children are framed in terms of time spent each day in MVPA. A value of ≥ 3600 cpm was originally used to define MVPA at the time of the data collection (Mattocks *et. al.,* 2008). More recently, following Evenson *et. al.* (2008), a lower cutpoint of ≥2296 has been calculated. Both sets of data are included, where *fg1203* - *fg1291* use a cut point of ≥3600 and *fg1300* - *fg1337* use a cut-point of ≥2296.

**Valid days**

At the time of writing (2018), the definition of a valid day of wear is generally between 480 to 600 minutes. There are two marker variables in the dataset: *fg1203* and *fg1300. fg1203* equals 1 when valid data is determined as at least 10 hours (600mins) of valid wear for at least 3 days. This threshold defines a valid day in variables *fg1205* to *fg1291. fg1300* summarises the number of valid days worn overall, based on 500 minutes of wear per valid day. This threshold defines a valid day in variables *fg1301* to *fg1337*.

Please note that the derivations using different cutpoints and valid day thresholds are clearly defined by the variable labels using the prefix ‘DV: ≥3600’ or ‘DV: ≥2296’.

Evenson K.R., Cattellier D., Gill K., Ondrak K., McMurray R.G. (2008) ‘Calibration of two objective measures of physical activity for children’. *Journal of Sports Science*. (26):1557–65.

Mattocks, C., Ness, A., Leary, S., Tilling, K., Blair, S.N., Shield, J., Deere, K., Saunders, J., Kirkby, J., Smith, G.D., Wells, J., Wareham, N., Reilly, John J. and Riddoch, C. (2008). ‘Use of accelerometers in a large field-based study of children: protocols, design issues and effects on precision’. *Journal of Physical Activity and Health*, 5 (1): S94-S107: https://doi.org/10.1123/jpah.5.s1.s98

**TF3 (age 15.5).**

The ActiGraph™ is a commonly used accelerometer in child and adolescent free-living physical activity studies. At the TF3 clinic, young people were asked to wear the ActiGraphTM accelerometer for 7 days, beginning the day after clinic attendance. Summary variables are included in the dataset. Reinvites have been excluded.

Below details the derived variables in the dataset that may be useful for analysis. Those interested in recoding the raw data are invited to contact ALSPAC.

**CPM**

Total physical activity is the total volume activity including activities at all intensities, measured as the average counts per minute (cpm) over the period of valid recording. This variable is used as it is the summary measure of total physical activity that has been validated against doubly labelled water. Associations with total physical activity are usually calculated per 100 cpm as this difference is of a similar order to the differences observed between males and females in these data.

**MVPA**

MVPA is the average minutes of moderate to vigorous physical activity per valid day. This variable is commonly used as current physical activity recommendations for children are framed in terms of time spent each day in MVPA. A value of >= 3600 cpm was originally used to define MVPA at the time of the data collection (Mattocks *et. al.,* 2008). More recently, following Evenson *et. al.* (2008), a lower cutpoint of >=2296 has been calculated. Both sets of data are included, where *fh5010* - *fh5078* use a cut point of >=3600 and *fh5100* – *fh5137* use a cut-point of >=2296.

**Valid days**

At the time of writing (2018), the definition of a valid day of wear is generally between 480 to 600 minutes. There are two marker variables in the dataset: *fh5073* and *fh5100. fh5073* equals 1 when valid data is determined as at least 10 hours (600mins) of valid wear for at least 3 days. This threshold defines a valid day in variables *fh5010* to *fh5078. fh5100* summarises the number of valid days worn overall, based on a minimum of 500 minutes of wear per valid day. This threshold defines a valid day in variables *fh5101* to *fh5137*.

Please note that the derivations using different cutpoints and valid day thresholds are clearly defined by the variable labels using the prefix ‘DV: ≥3600’ or ‘DV: ≥ 2296’.

Evenson K.R., Cattellier D., Gill K., Ondrak K., McMurray R.G. (2008) ‘Calibration of two objective measures of physical activity for children’. *Journal of Sports Science*. (26):1557–65.

Mattocks, C., Ness, A., Leary, S., Tilling, K., Blair, S.N., Shield, J., Deere, K., Saunders, J., Kirkby, J., Smith, G.D., Wells, J., Wareham, N., Reilly, John J. and Riddoch, C. (2008). ‘Use of accelerometers in a large field-based study of children: protocols, design issues and effects on precision’. *Journal of Physical Activity and Health*, 5 (1): S94-S107: https://doi.org/10.1123/jpah.5.s1.s98

**Age 24. Actigraph activity monitoring session**

For this session, participants were asked to wear an ActiGraph GT3X+ accelerometer device for four consecutive days, ideally starting the day after the clinic visit. This device provides an objective measurement of human activity.

The device is a small plastic box worn around the waist, just above the right hip. Participants were instructed to wear the device from first thing in the morning until they went to bed. They were advised to only take it off to avoid getting the device wet (e.g., swimming or bath/shower) or during physical contact sports to avoid damaging the device (e.g., rugby). To monitor wear times, YPs completed a diary of the times they wore and took off the device.

Participants were advised to wear the accelerometer devices if the following days were part of a ‘normal week’ with regards to the activity of the YP. If the participant was doing anything unusual in the days after the clinic, such as going on holiday, then the accelerometer was to be sent to them at an agreed future date.

The actigraph session was conducted as part of the SEACHANGE cardiovascular health project, with data collected between 17th November 2015 and 31st March 2017.

The cut-points used to distinguish different types of physical activity in the variables below are as follows (based on counts per minute; cpm):

* • \_S\_e\_d\_e\_n\_t\_a\_r\_y\_:\_ \_<\_1\_0\_0\_ \_c\_p\_m\_ \_
* • \_Light physical activity: 100-2020 cpm
* • \_Moderate-to-vigorous physical activity: >2020 cpm

Note that these cut-points are different from those previously used in ALSPAC as the participants are now adults. These cut-points have previously been used by Troiano *et al.* (2008), but if researchers would like to use different cut-points it is possible to reprocess the raw actigraph data (although additional fees may apply).

Valid days were operationalised as a wear time of at least 500 minutes, after excluding intervals of >60 minutes of zero counts. This follows previous protocols, and provides the most data per participant.

Note also that this physical activity data is based solely on data held in the device. The activity diaries completed by participants has not been processed, but the raw data is available upon request (although additional fees may apply).

Variables FKAC1010 to FKAC1110 detail physical activity over all days the device was worn, variables FKAC1200 to FKAC1300 detail physical activity over weekdays on which the device was worn, while variables FKAC1400 to FKAC1500 detail physical activity over weekend days on which the device was worn.

Troiano, R. P., Berrigan, D., Dodd, K. W., Masse, L. C., Tilert, T. & McDowell, M. (2008). Physical activity in the United States measured by accelerometer. Medicine and Science in Sports and Exercise, 40(1), 181-188.

**Analytic Plan**

1. **Step 1: Trajectory modeling of PA**. We will use group based trajectory modeling (GBTM)42 to define trajectories of MVPA from middle childhood through emerging adulthood for all participants with at least one PA assessment, using Maximum likelihood (ML) estimation with estimation maximization (EM). Following estimation, posterior class probabilities will be derived and used to assign individuals to classes. To estimate associations with DEx, we will use a “3-step approach.” First, the best fitting latent trajectory model is used to assign individuals to their most likely class using the predicted posterior probabilities of belonging to each class. These classifications will be saved (2nd step) and then included as predictors in the relevant new analyses (3rd step).
2. **Step 2: Associations with DEx**. We will estimate the association between PA trajectories with DEx and ED diagnoses (both at individual time points and lifetime risk by age 24) during adolescence using multivariable logistic regression models. We will assume outcome data were missing at random (MAR) conditionally on the variables included in the models which are associated with drop-out. We will use maximum likelihood estimation to account for missing data.
3. **Step 3: Sensitivity analyses.** We will complete sensitivity analyses to account for overlap in assessment timepoints between PA and ED variables. To do this, we will compute PA trajectories prior to age 16 (using accelerometer data only from ages 11, 13, 15) and determine whether these trajectories predict ED behaviors and diagnoses that onset at or after age 16.

**References**

1. Schaumberg K, Welch E, Breithaupt L, et al. The science behind the Academy for Eating Disorders’ Nine Truths about Eating Disorders. *Eur Eat Disord Rev*. 2017;25(6):432-450. doi:10.1002/erv.2553

2. Steinhausen HC. Outcome of eating disorders. *Child Adolesc Psychiatr Clin N Am*. 2009;18(1):225-242. doi:10.1016/j.chc.2008.07.013

3. Pisetsky EM, Thornton LM, Lichtenstein P, Pedersen NL, Bulik CM. Suicide attempts in women with eating disorders. *Journal of Abnormal Psychology*. 2013;122(4):1042-1056. doi:10.1037/a0034902

4. Smith AR, Fink EL, Anestis MD, et al. Exercise caution: over-exercise is associated with suicidality among individuals with disordered eating. *Psychiatry Res*. 2013;206(2-3):246-255. doi:10.1016/j.psychres.2012.11.004

5. Dalle Grave R, Calugi S, Marchesini G. Compulsive exercise to control shape or weight in eating disorders: prevalence, associated features, and treatment outcome. *Compr Psychiatry*. 2008;49(4):346-352. doi:10.1016/j.comppsych.2007.12.007

6. Carter JC, Blackmore E, Sutandar-Pinnock K, Woodside DB. Relapse in anorexia nervosa: a survival analysis. *Psychol Med*. 2004;34(4):671-679. doi:10.1017/S0033291703001168

7. Holtkamp K, Herpertz-Dahlmann B, Hebebrand K, Mika C, Kratzsch J, Hebebrand J. Physical activity and restlessness correlate with leptin levels in patients with adolescent anorexia nervosa. *Biol Psychiatry*. 2006;60(3):311-313. doi:10.1016/j.biopsych.2005.11.001

8. Greenwood BN, Foley TE, Le TV, Strong PV, Loughridge AB, Fleshner M. Long-term voluntary wheel running is rewarding and produces plasticity in the mesolimbic reward pathway. *Behav Brain Res*. 2011;217(2):354-362.

9. Stiles-Shields C, DclinPsy BB, Lock J, Le Grange D. The effect of driven exercise on treatment outcomes for adolescents with anorexia and bulimia nervosa: Driven Exercise and Adolescent Outcomes. *Int J Eat Disord*. 2015;48(4):392-396. doi:10.1002/eat.22281

10. Brewerton TD, Stellefson EJ, Hibbs N, Hodges EL, Cochrane CE. Comparison of eating disorder patients with and without compulsive exercising. *Int J Eat Disord*. 1995;17(4):413-416.

11. Shroff H, Reba L, Thornton LM, et al. Features associated with excessive exercise in women with eating disorders. *Int J Eat Disord*. 2006;39(6):454-461. doi:10.1002/eat.20247

12. Gielen M, Westerterp-Plantenga MS, Bouwman FG, et al. Heritability and genetic etiology of habitual physical activity: a twin study with objective measures. *Genes Nutr*. 2014;9(4):415. doi:10.1007/s12263-014-0415-5

13. Huppertz C, Bartels M, de Zeeuw E, et al. Individual Differences in Exercise Behavior: Stability and Change in Genetic and Environmental Determinants From Age 7 to 18. *Behav Genet*. 2016;46(5):665-679. doi:10.1007/s10519-016-9799-x

14. Anorexia Nervosa Genetics Initiative, Eating Disorders Working Group of the Psychiatric Genomics Consortium, Watson HJ, et al. Genome-wide association study identifies eight risk loci and implicates metabo-psychiatric origins for anorexia nervosa. *Nat Genet*. Published online July 15, 2019. doi:10.1038/s41588-019-0439-2

15. Greenwood BN, Foley TE, Le TV, Strong PV, Loughridge AB, Fleshner M. Long-term voluntary wheel running is rewarding and produces plasticity in the mesolimbic reward pathway. *Behav Brain Res*. 2011;217(2):354-362.

16. Heyman E, Gamelin FX, Goekint M, et al. Intense exercise increases circulating endocannabinoid and BDNF levels in humans—possible implications for reward and depression. *Psychoneuroendicrinology*. 2012;37(6):844-851.

17. Herring MP, O’Connor PJ, Dishman RK. The effect of exercise training on anxiety symptoms among patients: A systematic review. *Arch Intern Med*. 2010;170(4):321-331.

18. Greenwood BN, Strong PV, Loughridge AB, et al. 5-HT2C receptors in the basolateral amygdala and dorsal striatum are a novel target for the anxiolytic and antidepressant effects of exercise. *PLoS One*. 2012;7(9):e46118. doi:10.1371/journal.pone.0046118

19. Anderson E, Shivakumar G. Effects of exercise and physical activity on anxiety. *Front Psychiatry*. 2013;4:27.

20. Asmundson GJG, Fetzner MG, DeBoer LB, Otto MW, Smits JAJ. Let’s get physical: a contemporary review of the anxiolytic effects of exercise for anxiety and its disorders. *Depress Anxiety*. 2013;30(4):362-373. doi:10.1002/da.22043

21. Davis C, Kaptein S. Anorexia nervosa with excessive exercise: a phenotype with close links to obsessive-compulsive disorder. *Psychiatry Res*. 2006;142(2-3):209-217. doi:10.1016/j.psychres.2005.11.006

22. Cook B, Hausenblas H, Freimuth M. Exercise addiction and compulsive exercising: Relationship to eating disorders, substance use disorders, and addictive disorders. In: *Eating Disorders, Addictions, and Substance Use Disorders*. Eating Disorders. ; 2014:127-144.

23. Guarda AS, Schreyer CC, Boersma GJ, Tamashiro KL, Moran TH. Anorexia nervosa as a motivated behavior: Relevance of anxiety, stress, fear and learning. *Physiol Behav*. 2015;152 (B):466-472. doi:10.1016/j.physbeh.2015.04.007

24. Adams J. Understanding exercise dependence. *Journal of Contemporary Psychotherapy*. 2009;39:231-240.

25. Adams J, Kirkby RJ. Excessive exercise as an addiction: A review. *Addiction Research & Theory*. Published online 2002.

26. Bamber DJ, Cockerill IM, Rodgers S, Carroll D. Diagnostic criteria for exercise dependence in women. *British Journal of Sports Medicine*. 2003;37:393-400.

27. Bratland Sanda S, Martinsen EW, Rosenvinge JH, Rø Ø, Hoffart A, Sundgot Borgen J. Exercise dependence score in patients with longstanding eating disorders and controls: the importance of affect regulation and physical activity intensity. *European Eating Disorders Review*. 2011;19:249-255. doi:10.1002/erv.971/pdf

28. Davis C, Claridge G. The eating disorders as addiction: A psychobiological perspective. *Addict Behav*. 1998;23(4):463-475.

29. Herring M, Sailors M, Bray M. Genetic factors in exercise adoption, adherence and obesity. *Obes Rev*. 2014;15(1):29-39. doi:10.1111/obr.12089

30. Lichtenstein MB, Hinze CJ, Emborg B, Thomsen F, Hemmingsen SD. Compulsive exercise: links, risks and challenges facedent. *Psychol Res Behav Manag*. 2017;10:85-95. doi:10.2147/PRBM.S113093

31. Boyd A, Golding J, Macleod J, et al. Cohort Profile: the ’children of the 90s’--the index offspring of the Avon Longitudinal Study of Parents and Children. *Int J Epidemiol*. 2013;42(1):111-127. doi:10.1093/ije/dys064

32. Fraser A, Macdonald-Wallis C, Tilling K, et al. Cohort Profile: The Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. *Int J Epidemiol*. 2013;42(1):97-110. doi:10.1093/ije/dys066

33. Golding J, Pembrey M, Jones R, ALSPAC ST. ALSPAC--the Avon Longitudinal Study of Parents and Children. I. Study methodology. *Paediatr Perinat Epidemiol*. 2001;15(1):74-87.

34. Kann L, Warren CW, Harris WA, et al. Youth risk behavior surveillance--United States, 1995. *J Sch Health*. 1996;66(10):365-377.

35. Field AE, Taylor CB, Celio A, Colditz GA. Comparison of self-report to interview assessment of bulimic behaviors among preadolescent and adolescent girls and boys. *Int J Eat Disord*. 2004;35(1):86-92. doi:10.1002/eat.10220

36. Herle M, De Stavola B, Hübel C, et al. Eating behaviours in childhood and later eating disorder behaviours and diagnoses: a longitudinal study. *British Journal of Psychiatry*. Published online 2019. Accessed August 25, 2019. https://www.cambridge.org/core/journals/the-british-journal-of-psychiatry/all-issues

37. Micali N, Solmi F, Horton NJ, et al. Adolescent Eating Disorders Predict Psychiatric, High-Risk Behaviors and Weight Outcomes in Young Adulthood. *J Am Acad Child Adolesc Psychiatry*. 2015;54(8):652-659.e1. doi:10.1016/j.jaac.2015.05.009

38. Schaumberg K, Brosof LC, Lloyd EC, et al. Prospective associations between childhood neuropsychological profiles and adolescent eating disorders. *European Eating Disorders Review*. 2020;28(2):156-169. doi:10.1002/erv.2721

39. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Published online 2013.

40. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. *BMJ*. 2007;335(7612):194. doi:10.1136/bmj.39238.399444.55

41. House J, Eisler I, Simic M, Micali N. Diagnosing eating disorders in adolescents: a comparison of the eating disorder examination and the development and well-being assessment. *Int J Eat Disord*. 2008;41(6):535-541. doi:10.1002/eat.20528

42. Nagin DS, Odgers CL. Group-based trajectory modeling in clinical research. *Annu Rev Clin Psychol*. 2010;6:109-138. doi:10.1146/annurev.clinpsy.121208.131413