Published in final edited form as:

Horm Behav. 2013 July ; 64(2): 399–410. doi:10.1016/j.yhbeh.2013.02.019.

Puberty as a Critical Risk Period for Eating Disorders: A Review of Human and Animal Studies

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Abstract

Puberty is one of the most frequently discussed risk periods for the development of eating disorders. Prevailing theories propose environmentally mediated sources of risk arising from the psychosocial effects (e.g., increased body dissatisfaction, decreased self-esteem) of pubertal development in girls. However, recent research highlights the potential role of ovarian hormones in phenotypic and genetic risk for eating disorders during puberty. The goal of this paper is to review data from human and animal studies in support of puberty as a critical risk period for eating disorders and evaluate the evidence for hormonal contributions. Data are consistent in suggesting that both pubertal status and pubertal timing significantly impact risk for most eating disorders in girls, such that advanced pubertal development and early pubertal timing are associated with increased rates of eating disorders and their symptoms in both cross-sectional and longitudinal research. Findings in boys have been much less consistent and suggest a smaller role for puberty in risk for eating disorders in boys. Twin and animal studies indicate that at least part of the female-specific risk is due to genetic factors associated with estrogen activation at puberty. In conclusion, data thus far support a role for puberty in risk for eating disorders and highlight the need for additional human and animal studies of hormonal and genetic risk for eating disorders during puberty.

Keywords

puberty; eating disorders; anorexia nervosa; bulimia nervosa; ovarian hormones; estrogen; twin studies

Historically, puberty has been one of the most frequently discussed risk periods for the development of eating disorders (i.e., anorexia nervosa (AN), bulimia nervosa (BN)) and their symptoms (e.g., body dissatisfaction, weight concerns, dieting, binge eating). Traditional theories of risk focused on the psychosocial effects (e.g., increased body dissatisfaction) of the physical changes associated with puberty (e.g., increased adiposity) and their potential consequences for eating disorder development (Fornari & Dancyger 2003). However, human and animal data are converging to suggest that biological and genetic factors also significantly contribute to eating disorder risk during the pubertal transition. The overarching goal of this review is to evaluate the evidence in support of

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biological and genetic risk and synthesize these data with existing neuroendocrinological models of puberty's effects on behavior. Perhaps not surprisingly, most theories focus on gonadal hormones and their influence on sex-differentiated behaviors during and after puberty. This review will be no exception.

The review begins with an overview of the types of eating disorders and symptoms that have been examined in puberty studies. Data in support of puberty as a critical risk period for these phenotypes will then be reviewed, with a particular emphasis on differentiating pubertal status (i.e., pubertal stage at a given point in time) from pubertal timing (i.e., onset of puberty relative to peers, including early, on-time, and late onset) effects. Evidence from human and animal studies suggesting that biological and/or genetic factors contribute to puberty's effects will then be evaluated and integrated into existing behavioral neuroendocrinological models of sex-differentiated behaviors during puberty.

Eating Disorder Definitions

To date, studies of puberty have primarily focused on AN and BN and their component symptoms. DSM-IV criteria for each disorder (American Psychiatric Association, 2000) are presented in Table 1. Notably, two subtypes of AN exist, the restricting subtype which is characterized by strict dieting and/or excessive exercise only, and the binge/purge subtype which is characterized by strict dieting and/or excessive exercise as well as binge eating, purging, or binge eating and purging. Thus, despite common misconceptions, AN frequently includes binge eating and purging behaviors commonly thought to be exclusive to BN. Likewise, BN includes behaviors and cognitions that are commonly attributed to AN, including strict dieting and extreme concerns about shape/weight that significantly impact the individual's self-esteem (see Table 1). To avoid overlap between the two disorders, DSMIV stipulates that individuals with BN cannot be underweight (i.e., their weight must be > 85% of ideal), otherwise they would receive a diagnosis of AN, binge/purge subtype.

Both AN and BN are relatively rare disorders, with AN occurring in only .5% of the population and BN occurring in 1-3% (American Psychiatric Association, 2000). However, subthreshold cases of the disorders (see Table 1) are much more common with estimates as high as 10% (Fairburn and Bohn, 2005). These and other symptom presentations (i.e., those with binge eating disorder who binge eat but do not purge) are categorized as eating disorders not otherwise specified (EDNOS) within DSMIV (American Psychiatric Association, 2000). The fact that EDNOS diagnoses are the most frequently encountered eating disorders in clinical (Thomas et al., 2009) and community (Machado et al., 2007) samples has led the DSM 5 Workgroup to consider broadening the criteria for AN and BN to capture these more commonly encountered cases (Walsh, 2009).

The higher prevalence of EDNOS diagnoses also has led to a push for dimensional rather than categorical models of eating disorders and other forms of psychopathology. There is a growing recognition that categorical diagnoses may not accurately "carve nature at its joints" and that dimensional models (i.e., models that characterize patients based on quantitatively measured dimensions (e.g., degree of weight loss; frequency of binge/purge behaviors) rather than yes/no diagnoses) may get us closer to identifying the etiology of psychiatric disorders (Cuthbert, 2005; Krueger and Markon, 2011). Fortunately, because of the rarity of AN and BN, the eating disorders field has focused on dimensions of eating disorders for some time by examining symptoms of eating disorders (e.g., the tendency to binge eat, concerns about weight/shape, dissatisfaction with the size/shape of body parts) that are known to predate the onset of the full disorders (Jacobi et al., 2004) and cut across diagnostic boundaries of AN and BN. This has been particularly true of studies examining puberty that must account for the fact that full syndromal AN and BN are very rare before

puberty (see review below). Major dimensions of eating disorders that have been examined in studies of puberty are described in Table 1.

One final comment on eating disorder definitions is in order. Eating disorders are the most sex-differentiated disorders in our psychiatric nomenclature, as the female to male ratio ranges from 4:1 (Hudson et al., 2007) all the way up to 10:1 (American Psychiatric Association, 2000). Sex differences extend to the symptoms in Table 1 and have contributed to views that gonadal hormones may contribute to risk for eating disorders during puberty. This point will be further discussed later in the review, but suffice it to say that studies examining puberty's influence on eating disorder risk have focused more on female than male subjects.

Associations between Pubertal Status, Pubertal Timing, and Eating Disorders

Data over the last four decades have confirmed that puberty is a significant risk period for the development of eating disorders and eating disorder symptoms in girls. These studies have examined the frequency of eating disorders and their symptoms in terms of pubertal status (e.g., pre-puberty versus post-puberty) as well as pubertal timing (i.e., early, on-time, versus late maturers)¹. Most studies have examined these processes cross-sectionally, examining how pubertal status and/or timing at one point in time predict eating disorders and their symptoms. Although cross-sectional studies are important for understanding *proximal correlates* of the disorder, longitudinal/prospective studies are needed to ensure that pubertal status/timing are *risk factors* for eating disorders even after all girls “catch up” and have completed their pubertal development. Persistence of pubertal status and timing effects can be examined via: 1) longitudinal/prospective studies that examine whether pubertal status/timing effects at time 1 predict later risk at time 2, particularly when time 2 occurs in post-puberty; and/or 2) retrospective studies that assess whether recalled markers of pubertal development (e.g., menarche) occurred earlier or later than peers and/or population norms. The later studies are obviously less rigorous, as they rely on retrospective reports that are prone to memory biases (Coughlin, 1989). Nonetheless, rare disorders like eating disorders can be difficult to investigate in prospective studies due to the small number of expected cases, and so most studies of clinical eating disorders rely on retrospective reports.

Notably, it remains an open question whether persistence of status effects reflect processes that are independent of pubertal timing, i.e., since all girls eventually achieve advanced pubertal development, longitudinal effects of pubertal status may simply reflect the timing of these processes (i.e., early or late) at the time of initial assessment. These points highlight the fact that although persistence of puberty's effects across time provides strong support for pubertal processes as risk factors, they cannot disentangle pubertal status from pubertal timing as the critical mechanisms underlying the effects.

Despite these caveats, overall, findings from cross-sectional and longitudinal studies are remarkably consistent in suggesting that pubertal status and timing effects persist across time and are associated with a significantly increased risk of developing eating disorders and their component symptoms in girls, although findings are much less clear in boys.

Girls

Eating Disorder Diagnoses—Two types of studies have examined the effects of puberty on risk for AN, BN, and EDNOS. The first indirectly examined the influence of puberty by exploring rates of eating disorders in children versus adolescents. These studies consistently

show a significantly increased prevalence of all forms of eating disorders in individuals in mid-late adolescence as compared to pre-adolescence (Bulik, 2002). Indeed, pre-pubertal onset of eating disorders is rare (Bulik, 2002), and mean ages of onset for the disorders (i.e., 15–19 years for AN and BN) (American Psychiatric Association, 2000; Favaro et al., 2009; Favaro et al., 2003) reflect a post-pubertal bias in onset.

Nonetheless, several psychosocial and biological events take place between childhood and adolescence, leaving a specific role for puberty unclear. The second type of study directly examined rates of eating disorders by pubertal status and timing. More of these investigations have examined pubertal timing than pubertal status, likely due to the difficulty of capturing new onset cases during pubertal development. Studies thus far consistently suggest significant associations between pubertal status/timing and both BN and EDNOS (see Table 2). Girls who are at more advanced stages of pubertal development have increased rates of both disorders, even after controlling for age. Likewise, with few exceptions, a higher percentage of early maturers are among those diagnosed with BN as compared to women without eating disorders. This pattern of results is observed in combined samples of AN and BN women as well (see Table 2). Importantly, although two prospective studies failed to find an effect of pubertal status (Killen et al., 1994) or timing (Stice et al., 2001) on risk for BN, findings from retrospective studies clearly show that the effects of early pubertal timing on BN persist across late adolescence (Biederman et al., 2007; Graber et al., 1997; Kaltiala-Heino et al., 2003; Kaltiala-Heino et al., 2001; Ruuska et al., 2003) into young (Corcos et al., 2000; Fairburn et al., 1997; Romans et al., 2001) and middle (Romans et al., 2001) adulthood.

Results for AN only have been more mixed. Although some studies find early maturers are at increased risk for AN (see Table 2), even when assessed in adulthood (Crisp, 1970; Nicholls and Viner, 2009), many failed to find an effect, or found a higher prevalence of *late* maturers in AN samples (Root et al., 2011). No studies have examined differential rates of AN across pubertal status. The general lack of support for pubertal effects on AN may be due to the relatively small number of studies conducted and/or the difficulty of studying early-onset AN that has a much lower prevalence (i.e., .5%) than BN (i.e., 1-3%) or EDNOS (i.e., ~10%) (American Psychiatric Association, 2000). In addition, because extreme dieting frequently begins months/years before AN onset and can forestall pubertal development (Lantzouni et al., 2002; Roze et al., 2007), disentangling the effects of the disorder on puberty versus the effects of puberty on the disorder can be difficult. This tends to be less of an issue for BN and EDNOS where the dieting is less extreme and other core symptoms (e.g., binge eating, purging) tend not to disrupt pubertal processes.

Eating Disorder Symptoms—Studies have investigated component symptoms of eating disorders (e.g., body dissatisfaction, dieting; see Table 1) as well as global measures that sum across items tapping body dissatisfaction/weight concerns, binge eating, and purging/non-purging behaviors. These global measures assess the overall likelihood of developing eating disorders given that these symptoms are known risk factors for AN and BN (Jacobi et al., 2004). Nevertheless, given that global measures frequently do not include low body weight as an indicator, these measures likely tap BN or EDNOS pathology more than AN *per se*.

Most studies have found significant effects of both pubertal status and timing on global as well as specific eating disorder symptoms (see Table 2). With few exceptions, studies tend to find higher levels of symptoms in girls at more advanced stages of pubertal development, particularly when comparing pre-early puberty to mid-late puberty (e.g., Culbert et al., 2009; Klump et al., 2007a). Pubertal timing results largely replicate these results where the highest rates of eating disorder symptoms are found in early maturing as compared to on-

time and late-maturing girls (see Table 2). Findings have been particularly robust for body dissatisfaction and weight/shape concerns where studies are numerous and negative findings have been relatively rare (for interesting exceptions, see (Brooks-Gunn and Warren, 1988) and (Slap et al., 1994) showing positive associations between breast development and body satisfaction).

Although most studies of both pubertal timing and status have been cross-sectional in nature, some prospective and retrospective studies have examined persistence across time. With some exceptions (Leon et al., 1993; Leon et al., 1995; McCabe and Ricciardelli, 2004), pubertal timing effects have been observed in late (Baker et al., 2012; Graber et al., 1994; Harden et al., 2012; Hayward et al., 1997; Ohring et al., 2002; Oinonen and Bird, 2012) as well as young (Ackard and Peterson, 2001; Graber et al., 1994; Keski-Rahkonen et al., 2005; Ohring et al., 2002; Petersen et al., 1994; Reichborn-Kjennerud et al., 2004; Striegel-Moore et al., 2001; Tenconi et al., 2006; Zehr et al., 2007) and middle (Johansson and Ritzen, 2005) adulthood. Several studies were prospective and found that timing effects assessed during puberty persisted one to 30 years after initial assessment. Prospective studies of pubertal status have been fewer in number (Attie and Brooks-Gunn, 1989; Cattarin and Thompson, 1994; Field et al., 1999; The McKnight Investigators, 2003; Keel et al., 1997; McCabe and Ricciardelli, 2004), but many found that advanced pubertal development at the time of initial assessment predicted eating disorder symptoms 8 months to 3 years later (Field et al., 1999; Keel et al., 1997; McCabe and Ricciardelli, 2004).

Boys

Far fewer studies have examined the effects of puberty on eating disorders in males (see Table 2) and to date, findings are quite mixed. Similar to results in girls, 22 studies found that early maturing boys and/or those at advanced stages of puberty had higher rates of AN, BN, and eating disorder symptoms (see Table 2). Results have been most consistent for body dissatisfaction and weight/shape concerns where several studies found significant effects of pubertal status and timing.

However, 13 studies failed to find significant effects of pubertal status/timing on BN or disordered eating symptoms (see Table 2), four studies found that *late* maturers had higher rates of body dissatisfaction (McCabe and Ricciardelli, 2004; Michaud et al., 2006; Petersen et al., 1994; Siegel et al., 1999), and five studies found that advanced pubertal development was associated with *improved* body image (McCabe et al., 2001; Suka et al., 2005), *enhanced* self-concept (O'Dea and Abraham, 1999a, 1999b), and/or *increased* perceptions of physical attractiveness and/or *decreased* social pressures around eating (Muris et al., 2005).

Results from prospective and retrospective studies examining persistence across time were also equivocal. While four studies found early maturers to be at increased risk for eating disorder symptoms into late adolescence/young adulthood (Domine et al., 2009; McCabe and Ricciardelli, 2004; Nielsen, 1985; Zehr et al., 2007), three studies failed to find an effect of early pubertal timing on eating disorder risk during these later time periods (Keski-Rahkonen et al., 2005; Leon et al., 1995; Reichborn-Kjennerud et al., 2004). Only one prospective study of pubertal status found persistence of effects (Baker et al., 2012) while others found no significant associations between advanced pubertal development at time 1 and later risk for eating disorders at time 2 (Keel et al., 1997; Ricciardelli and McCabe, 2003).

Summary

Overall, results are relatively consistent in girls showing significant effects of both pubertal status and timing on most eating disorder phenotypes. The strongest effects have been

observed for BN and its symptoms, including body dissatisfaction, weight/shape concerns, binge eating, and purging. Findings for AN have been much less consistent, although studies are fewer in number and the trajectory of the disorder makes it more difficult to detect pubertal effects. Nonetheless, the consistency of results for BN and eating disorder symptoms is striking given study differences in the eating constructs measured (e.g., weight concerns versus binge eating) and pubertal measures (i.e., self-reports of secondary sex characteristics, physician ratings of development, age at menarche). These data provide strong support for a role for puberty in the etiology of these clinical phenomena in humans.

Findings for boys have been much more mixed. Several studies show no effect of pubertal status/timing on eating disorders and their symptoms, and persistence of associations across time has not been established. The lone exception might be body dissatisfaction and weight/shape concerns where the majority of studies show positive effects of both status and timing. However, only two studies examined persistence across time, and their findings were discrepant (i.e., Zehr et al. (2007) found persistence while Keski-Rahkonen et al. (2005) did not). Moreover, advanced pubertal development has been associated with *positive* as well as negative body image in boys (see above). Overall, the bulk of the data suggest that puberty is likely to play a much larger role in eating disorder risk in girls than boys and that sex-specific processes during puberty may differentially contribute to eating disorders in females versus males.

Mechanisms underlying Puberty's Effects on Eating Disorder Risk

Prevailing theories of risk have posited that significant pubertal status and timing effects in girls are due to the physical changes of puberty and their effects on body satisfaction, self-esteem, and mood (Bulik, 2002; Fornari and Dancyger, 2003). These theories emphasize the role of body dissatisfaction in causing increased dieting that then leads to AN and BN. Early maturers are thought to be at particular risk given that they experience these physical changes earlier than their peers and may therefore experience even more body dissatisfaction than their developmentally on-time counterparts. Girls are believed to be at increased risk relative to boys given that pubertal physical changes in girls (i.e., increased adiposity) move them away from beauty ideals, while physical changes in boys (i.e., increased muscle mass) move them closer to their beauty ideals (Bulik, 2002; Fornari and Dancyger, 2003).

Although data testing the full psychosocial model are relatively sparse, some studies have supported its major tenants, at least in regard to the association between pubertal status, body dissatisfaction, and dieting (Attie and Brooks-Gunn, 1989; Bulik, 2002; Gralen et al., 1990). However, no studies have examined whether these processes ultimately lead to the development of AN or BN, and researchers are beginning to consider biological/genetic influences as well. The pubertal activation of ovarian hormones and their substantial role in sex-differentiated behaviors have made this system a prime candidate in the hunt for biological factors underlying pubertal risk. Emerging data from both human and animal studies are providing support for these hypotheses.

Human Studies

Twin Studies of Adolescence—Initial hints that biological and/or genetic factors might be important for pubertal risk in girls came from twin studies examining developmental differences in genetic influences on eating disorder symptoms during adolescence. These studies examined global measures (assessing body dissatisfaction, weight concerns, binge eating, and compensatory behaviors) as well as specific eating disorder symptoms (e.g., body dissatisfaction, weight concerns) and found significant increases in genetic influences across adolescence, where there was essentially no genetic influence (i.e., 0% heritability)

on eating disorder symptoms in pre-adolescent female twins (age 11), but significant genetic effects (~50% heritability) in twins during late adolescence (age 17) (Klump et al., 2010a). Two follow-up studies confirmed that developmental changes emerged between pre-adolescence and middle adolescence (Klump et al., 2007a; Klump et al., 2010a), as increases in genetic effects (from 0% to ~50%) were only observed between early and middle adolescence (i.e., between ages 11 and 14), while the magnitude (~50% heritability) and type of genetic factors (Klump et al., 2007a) remained constant from mid-adolescence (i.e., age 14) into middle adulthood (up to age 41). Developmental differences were observed in both cross-sectional (Klump et al., 2010a; Klump et al., 2000) and longitudinal (Klump et al., 2007a) studies, suggesting that the effects were robust and reflected within-twin pair shifts in etiologic influences across adolescence. The pattern of results remained unchanged after controlling for body mass index (BMI) and mood symptoms (e.g., anxiety) (Klump et al., 2007a; Klump et al., 2000), suggesting that the developmental differences were specific to eating disorder symptoms rather than secondary changes due to developmental differences in correlated phenotypes. Finally, the lack of changes in magnitude or type of genetic influences after mid-adolescence further highlighted processes specific to the early adolescent period as key to genetic (and likely phenotypic) risk for eating disorders.

Twin Studies of Puberty—Given that puberty typically begins between pre-adolescence and middle adolescence in girls, puberty was an obvious candidate for studies examining mechanisms underlying age differences in genetic risk. Twin studies took up the cause and began investigating whether shifts in genetic effects occur across puberty rather than across adolescent ages *per se*. Instead of dividing twins by age, these studies examined differences in genetic risk in girls who varied in their pubertal status and/or timing, as assessed via secondary sex characteristics (e.g., breast development, hair growth, onset of menses).

Most studies of pubertal status used a 2-group analysis that compared twins in pre-early puberty to those in mid-post puberty (Culbert et al., 2009; Klump et al., 2003), although one study examined changes across the full range from pre-puberty to post-puberty (Klump et al., 2007b). Regardless of the grouping method used, substantial differences in genetic effects across pubertal status were observed, such that genes accounted for 0% of the variance in eating disorder symptoms (e.g., overall levels, body dissatisfaction, weight concerns) in pre-early puberty, but ~50% of the variance during mid-puberty and beyond. Increases in genetic effects were found to be linear across puberty (Klump et al., 2007b), although changes were complete by the onset of menses (Culbert et al., 2009; Rowe et al., 2002; Silberg and Bulik, 2005). All studies of puberty were cross-sectional, not longitudinal; however, pubertal differences in genetic effects persisted even after controlling for age and BMI (Culbert et al., 2009; Klump et al., 2003), and there were no changes in the degree of genetic influence from post-puberty through late adolescence (i.e., heritability was ~50% from post-puberty on) (Klump et al., 2003). These data strongly suggest that puberty accounts for age differences observed previously and that there may be genetic links between processes occurring during puberty and eating disorder symptoms in girls.

Two recent twin studies of pubertal timing confirmed that this is the case. Baker et al. (in press) and Harden et al. (2012) directly examined these genetic links by investigating shared genetic risk factors between eating disorder symptoms (e.g., overall eating disorder symptoms, dieting) and age at menarche or early pubertal timing, respectively. Associations between these menarche variables and eating disorder symptoms were due to a shared set of genetic risk factors contributing to both phenotypes. Importantly, after controlling for these shared genetic risk factors, phenotypic associations between early pubertal timing and dieting were eliminated, suggesting that genetic risk factors (rather than environmental influences) entirely account for the co-occurrence of early menarche and eating disorder behaviors in girls (Harden et al., 2012).

Overall, data from twin studies provide strong support for puberty as a period of significant genetic risk for eating disorders. Genetic influences appear to become “activated” during the pubertal period and may increase phenotypic risk for the disorders in girls. These results are leading to a re-thinking of traditional theories of pubertal risk focusing on environmental mechanisms (see above) as well as renewed interest in ovarian hormones (most notably, estrogen) as potential risk factors that are activated during puberty and may drive increases in, and genetic risk for, eating disorder symptoms during the critical pubertal period.

Twin Studies of Estrogen—Researchers cite several lines of evidence in support of a focus on estrogen (Klump et al., 2010b). For example, estradiol release during puberty closely mimics pubertal activation of genetic effects on eating disorder symptoms. Although estrogen is present at low levels in girls prior to puberty, the activation of the GnRH pulse generator during pre-puberty leads to linear increases in ovarian secretion of estradiol across puberty (Wilson et al., 1998). This pattern of release is similar to the increases in genetic influences on disordered eating across puberty (Klump et al., 2007b) and is in contrast to the activation of the other primary ovarian hormone, progesterone, which increases only after first ovulation. Given twin study data showing increases in genetic effects around mid-puberty (Culbert et al., 2009; Klump et al., 2003) and before menarche, progesterone is not viewed as a major player in phenotypic and genetic risk for disordered eating during the pubertal period (Klump et al., 2010b).

Estrogen also drives many of the pubertal changes in secondary sex characteristics (e.g., breast development) (Wilson et al., 1998) that have been shown to moderate genetic influences on eating disorder symptoms. Indeed, developmental twin studies showing increased genetic effects (see above) relied on assessments of these secondary sex characteristics for assessing pubertal development. The fact that estrogen causes the physical changes that have been found to moderate genetic influences on DE has led to suggestions that estrogen might be one of the mechanisms underlying puberty’s effects on genetic risk (Klump et al., 2010b).

Finally, researchers have highlighted the fact that one of the primary functions of estrogen and other steroid hormones is to regulate gene transcription, and thereby protein synthesis, within the central nervous system (Ostlund et al., 2003; Wilson et al., 1998). Some of the genes regulated by estrogen have been found to be significantly associated with eating disorders, particularly those in the serotonin system (Hildebrandt et al., 2010; Ostlund et al., 2003) and those associated with brain-derived neurotrophic factor (BDNF) (Klump & Culbert, 2007). Researchers have proposed (Klump and Culbert, 2007; Klump et al., 2010b) that increases in estrogen at puberty may contribute to genetic risk via the hormones’ effects on the production of these important neurotransmitters/neurotrophins, their receptors, and/or their signal transduction mechanisms. Moreover, variants of ovarian hormone receptor genes (e.g., estrogen receptor beta) (Klump and Gobrogge, 2005) may increase risk for binge eating by causing different patterns of gene regulation by ovarian hormones, leading to distinct cellular and behavioral responses. In these scenarios, individual differences in the production of ovarian hormones are not of consequence – the key individual difference variable is the presence or absence of susceptibility alleles that are regulated by ovarian hormones. These individual differences would become evident after ovarian hormone activation (i.e., after puberty).

To date, only one pilot study has investigated this possibility, and it did so indirectly using a twin study design. Klump et al. (2010) compared the magnitude of genetic effects on disordered eating in twins with high (i.e., above the median value) versus low (i.e., below the median value) estradiol levels during puberty. Results suggested significant differences in genetic influences on overall eating disorder symptoms by estradiol levels, with no

genetic influence in twins with low estradiol levels but significant genetic effects in twins with high estradiol levels. Findings remained unchanged after controlling for age and BMI, suggesting direct effects of estrogen on genetic risk for eating disorders during puberty in girls. Most importantly, results remained unchanged after controlling for changes in secondary sex characteristics, suggesting that differences in estradiol account for differences in genetic effects across puberty in previous studies.

Clearly, additional research is needed to replicate these results, particularly given the small sample size ($N = 99$ twin pairs) for this pilot twin project. However, corroborating data come from twin studies of males examining the effects of puberty on genetic risk for disordered eating (Klump et al., 2012). Boys do not experience increases in estrogen during puberty, as their pubertal development is driven primarily by increases in testosterone. If pubertal increases are present in boys, then factors other than (or in addition to) estrogen may drive increases in phenotypic and genetic effects in girls. In contrast to findings in girls, results showed no changes in genetic effects on overall levels of disordered eating in male twins across pre-early puberty, mid-late puberty, or young adulthood. The heritability remained constant at ~50% of the variance in all groups (Klump et al., 2012). These findings strongly suggest that pubertal increases in genetic influences are specific to girls and may be related to the estrogen effects described above.

Summary—Findings from twin studies provide support for a role for genetic factors in pubertal risk for eating disorders in girls. Dramatic increases in genetic effects have been observed across adolescence that appear to be due to estrogen activation during puberty. These changes are not present in boys, providing further, indirect support for pubertal hormone influences on risk for eating disorders in girls. Finally, emerging data confirm that associations between early pubertal timing and key disordered eating symptoms are due to genetic (rather than environmental) risk factors.

Although these studies do not rule-out psychosocial explanations for pubertal risk, they call into question the predominance of these risk factors in etiologic models of risk. Harden et al. (2012) showed rather convincingly that phenotypic associations between early pubertal timing and key eating disorder symptoms (e.g., dieting) are eliminated when within-family, genetic risk factors are controlled. Likewise, twin studies of puberty that control for age and BMI, and the twin study of estrogen that controlled for age, BMI, and the physical changes of puberty, suggest direct effects of puberty and estrogen on genetic and phenotypic risk.

Animal Studies

Nonetheless, it is difficult to control for all potentially relevant psychosocial risk factors in human studies, as the level of experimental control is necessarily limited. Animal studies can be helpful in these cases for teasing apart biological/genetic from psychosocial/environmental risk and identifying causal mechanisms. To date, only one study has examined the effects of puberty on eating disorder risk in animals by investigating whether pubertal increases in eating disorder symptoms observed in girls are present in female animals as well. Klump et al. (2011) used the binge eating resistant/binge eating prone rat model of binge eating (Boggiano et al., 2007) to determine if binge eating proneness (i.e., the tendency to consistently consume large amounts of palatable food (i.e., food that is high in fat and/or sugar) in a short period of time) emerges during puberty in female rats. The focus on binge eating was predicated on the fact that binge eating is a key eating disorder phenotype that is disrupted in both AN and BN and is easier to model in animals than the cognitive features of the disorders (Klump et al., 2011b).

Klump et al. (2011) found that differences in palatable food intake between binge eating prone and binge eating resistant rats (i.e., rats who consistently consume smaller amounts of

palatable food in a short period of time) in adulthood did not emerge until puberty. In pre-puberty, there were no significant differences in PF consumption between the two groups of rats, but significant differences emerged during mid-late puberty and persisted into adulthood. Importantly, the two groups did not differ in their chow intake or body weight at any stage of development, suggesting that the pubertal effects were specific to palatable food intake and binge eating phenotypes. Findings were replicated across two independent samples of rats.

Notably, these findings are unlikely to be due to environmental or psychosocial influences, as female rats do not experience key psychosocial/psychological risk factors (i.e., increased body dissatisfaction) that are present in humans. However, data showing that these effects are due to ovarian hormones (and estrogen in particular) are lacking, as this observational study did not manipulate ovarian hormones. Nonetheless, indirect data from animal studies of food intake support a role for ovarian hormones in these effects. These studies date back more than 40 years and convincingly show that estrogen inhibits food intake in adult female rats and other species, but these causal effects do not emerge until puberty (Asarian and Geary, 2006; Swithers et al., 2008; Wade, 1976). Before puberty, exogenously administered estradiol does not have any effect on food intake in female rats (Asarian and Geary, 2006). The same pubertal pattern has been observed for food intake patterns that are typical of binge eating episodes (e.g., preference for sweet foods); female rats' preference for sweet solutions (relative to males) are mediated by estrogen in adulthood, but these sex differences do not emerge until puberty (i.e., male and female rats do not differ in preference for sweet solutions prior to puberty) (Wade, 1976).

Summary, Integrative Theories and Future Directions

In summary, data from humans are clear in showing that both advanced pubertal status and early pubertal timing significantly increase risk for eating disorders (particularly BN and EDNOS) and their symptoms in girls. Findings further suggest that these effects are at least partially genetically mediated via the effects of estrogen during puberty. Animal studies are fewer in number, but results thus far support a role for biological factors (and possibly estrogen) in pubertal risk for binge eating phenotypes. Although additional animal and human studies are clearly needed (see below), findings thus far are sufficient to begin integrating current data with existing hormonal theories of pubertal risk for behavioral phenotypes.

Integrative Theories

An ideal framework for conceptualizing pubertal and hormonal risk for eating disorders is the activational and organizational theory of hormone action on sex-differentiated behavior. This theory posits two types of gonadal hormone effects on behavior: activational (i.e., transient effects that depend on the presence/absence of hormone) versus organizational (i.e., permanent effects that persist beyond the period of exposure to hormone and program later activational responses to hormone) influences. To date, no studies have directly compared the influence of these two hormone effects for eating disorders, although data support the possible importance of both for eating disorder risk during puberty. For example, estrogen exhibits robust activational effects on eating disorder symptoms in adulthood, where it is inversely correlated with food intake (Buffenstein et al., 1995), binge eating (Edler et al., 2007; Klump et al., 2008; Klump et al., 2013), and weight concerns (Racine et al., 2012) in women, and food intake (Asarian and Geary, 2006), binge eating (Babbs et al., 2011; Yu et al., 2008), and preference for sweet foods (Wade, 1976) in adult female animals. These data would suggest that increases in phenotypic and genetic risk for eating disorders by pubertal status may be due to increased levels of circulating estrogen starting early in puberty and continuing through adulthood.

However, if estrogen's effects were purely activational in nature, we would expect significant phenotypic associations between estradiol levels and eating disorder symptoms in girls during puberty, as levels of eating disorder symptoms should correlate with circulating levels of estradiol. This association has not been observed, as correlations between estradiol levels and eating disorder symptoms (e.g., body dissatisfaction, binge eating) during puberty have been small and non-significant (Nottelmann et al., 1986; Slap et al., 1994; Warren and Brooks-Gunn, 1989). This is in contrast to significant and moderate associations between disordered eating symptoms and estradiol levels in adult women (Edler et al., 2007; Klump et al., 2008; Klump et al., 2013; Racine et al., 2012).

These differential phenotypic associations across development fit nicely with the organizational hypothesis of gonadal hormone action during puberty which predicts: 1) hormones organize behavior during puberty through permanent changes in brain structure/function; and 2) these changes organize the brain to respond to circulating levels of hormones in adulthood which activate and/or influence the expression of behavior (Sisk and Zehr, 2005). Indeed, when hormone organizational effects are present, little-to-no phenotypic association between hormones and behavior is observed before/during puberty, whereas phenotypic associations are present in adulthood (Sisk and Zehr, 2005). Another key component of this theory is that organizational effects cause permanent changes in behavior that persist beyond the initial period of organization and are relatively immutable to hormone manipulations in adulthood. The pubertal timing effects described above fit with this aspect of the theory, as several studies have found that early maturers report elevated levels of eating disorder symptoms well into adulthood. New animal data provide additional support for this possibility, as the binge prone phenotypes that emerge during puberty in rats are immutable to ovarian hormone manipulations in adulthood, i.e., they persist in adulthood even after the removal of the primary source of estrogen via ovariectomy (Klump et al., 2011a). Thus, they are permanent phenotypes that are organized at puberty and continue into adulthood. Finally, in terms of general food intake, estradiol treatment fails to alter chow intake in female animals that are ovariectomized prior to puberty, whereas predictable changes in food intake are observed with exogenous estradiol treatment in animals ovariectomized in adulthood (Asarian and Geary, 2006; Wade, 1976). Thus, at least for food intake, the presence of ovarian hormones during puberty is required for the activational effects of estrogen on food intake in adulthood. Pubertal ovarian hormones appear to organize the brain in order to respond to the activating effects of estrogen on food intake (and possibly eating disorder symptoms) in adulthood.

Future Directions

Although still in its infancy, research on biological and genetic influences on pubertal risk for eating disorders has made great strides in confirming the likely presence and importance of these effects, as well as highlighting several areas in need of future research. On the phenotypic side, it will be important for future studies to disentangle the long-term effects of pubertal status from pubertal timing. As noted previously, it is currently unknown whether the persistence of status effects reflects an actual effect of pubertal status at the time of initial assessment or the relative timing of that development in relation to peers. Studies could disambiguate these processes by comparing the longitudinal effects of initially assessed pubertal status (i.e., pre-, mid-, late-puberty) to the effects of pubertal timing (i.e., early versus late timing, defined using within-sample distributions of pubertal status at the time of initial assessment and/or population norms). Such data could clarify potential differences in the proximal versus the long-term effects of pubertal status and timing on eating disorder risk.

Much more data are needed on pubertal status/pubertal timing effects on AN and its symptoms. This area can be most fruitfully tackled using a combination of animal and

human studies that can maximize inferential power as well as ecological validity. It would be helpful to examine symptoms that are specific to AN (i.e., extreme weight loss and dieting) rather than those common to both AN and BN (i.e., body dissatisfaction, weight concerns) to determine if puberty's effects extend to the AN spectrum as well. Investigators are currently focusing on the activity-based anorexia (ABA) animal model (Aoki et al., 2012) and examining whether the phenotype emerges during puberty and the neural substrates underlying pubertal risk. This line of work is likely to produce the type of AN-specific data that is currently lacking in the field.

Likewise, more studies are needed on the effects of puberty on binge eating disorder (BED) and EDNOS. BED will be a new disorder in DSM 5, and EDNOS diagnoses are of significant interest due to their increased prevalence in the population (relative to AN and BN). To some extent, the dimensional approach of most studies ameliorates concerns about the lack of data, as key symptoms contributing to these diagnoses (e.g., binge eating, dieting) show the pubertal phenotypic and genetic effects described herein. Nonetheless, given the later age of onset of BED and a need to more clearly demarcate similarities/differences between this disorder and other well-established eating disorders, future phenotypic and genetic studies should examine puberty's effects on BED/EDNOS and their early precursors (e.g., loss of control over eating) to determine the role of puberty in their development.

With regard to genetic and hormonal mechanisms, more twin studies of estrogen are clearly needed to replicate initial pilot data and confirm a role for estrogen in pubertal emergence of phenotypic and genetic risk for eating disorders. Longitudinal studies would go a long way in this regard, as these studies could determine whether *within-person changes* in phenotypic and genetic risk across puberty are due to estrogen activation. Much like studies of puberty, these studies should more clearly differentiate status versus timing effects to determine if estrogen levels alone, or early versus late exposure to estrogen, is important. Studies thus far suggest that both types of effects might be operating, as Klump et al. (2010) found that higher estrogen levels during puberty (i.e., status effects) significantly increased genetic effects on disordered eating, regardless of age (i.e., the impact of low/high estrogen levels did not depend on the twin's age). By contrast, Harden et al. (2012) and Baker et al. (in press) found that early pubertal timing shared genetic risk factors with eating disorder symptoms, suggesting that timing of puberty (and possibly, timing of estrogen activation) might influence genetic risk for eating disorders. More twin studies directly examining status versus timing effects of estrogen activation are clearly needed to confirm these impressions.

It would be helpful for these studies to also examine other phenotypes that are comorbid with eating disorders and have been linked to pubertal processes (e.g., depression, anxiety, substance use). Some developmental twin studies show that changes in genetic risk for disordered eating are independent of mood, but most studies have not examined comorbid psychiatric traits. Additional research into the specificity of puberty/hormone effects for eating disorders will help clarify etiologic models of, and pathways for, eating disorders and inform dimensional models of psychopathology. Ideally, these investigations would identify similarities as well as differences in hormone effects across disorders to more clearly delineate processes that predict differential disorder expression (e.g., common genetic/hormonal mechanisms for a range of pathology that then interact with disorder-specific environmental risk factors (e.g., pressures for thinness) (see Kendler et al., 2010 for data suggesting the presence of common genetic versus disorder-specific environmental risk factors).

Clearly, additional studies are needed to directly examine the significance of activational versus organizational influences of estrogen on eating disorder phenotypes during puberty. Animal studies would be very useful in this regard, as they could examine risk for eating disorder phenotypes in female animals differentially exposed to ovarian hormone manipulations across development. For example, if estrogen influences risk for eating disorders via its organizational properties, one would expect decreases in eating disorder phenotypes in pre-pubertally ovariectomized animals that cannot be restored with hormone treatment in adulthood. These animals would be permanently altered to be low risk phenotypes in adulthood, regardless of ovarian hormone exposure in later life.

However, human studies of developmental periods other than puberty could also increase understanding of organizational versus activational influences. If estrogen has only activational influences on eating disorder risk, we would expect changes in phenotypic and genetic risk for eating disorders across the menstrual cycle and after menopause. In terms of the menstrual cycle, we should see robust changes in eating disorder symptoms and genetic risk across menstrual cycle phases that are due to differential hormone activation across the cycle. In terms of menopause, we should see significant changes in phenotypic and genetic risk for eating disorders after menopause when the ovarian hormone system is de-activated in women. By contrast, if estrogen's influence is primarily organizational, we would expect much less of a change in phenotypic and genetic risk for eating disorders and their symptoms across the menstrual cycle and in later life. In this case, the "turning on" of genes during puberty would cause permanent changes in gene action and/or brain structure/function that make the eating disorder phenotype relatively immutable to changes in hormone concentrations across the adult reproductive cycle. Indirect data exist to support both possibilities, as phenotypic changes in symptoms (albeit, somewhat modest) are observed across the menstrual cycle (Edler et al., 2007; Klump et al., 2008; Klump et al., 2013; Racine et al., 2012), and significant eating disorder symptoms persist in women over the age of 50 (Gagne et al., 2012). However, no studies have directly compared genetic risk across menstrual cycle phase or pre- versus post- menopause. Data from such investigations would provide critical insights into the relative importance of activational versus organizational influences of ovarian hormones on risk for eating disorders.

Studies of the prenatal/perinatal period are also needed, as recent studies show that the effects of estrogen during puberty may depend upon earlier organizational influences of testosterone during prenatal/perinatal development. These theories posit that it is the absence of prenatal testosterone, and the presence of pubertal estrogen, that organizes sex-specific behavior in females (Bell and Zucker, 1971; Gentry and Wade, 1976). Intriguing new data suggest that these processes may be critical for eating disorders, as sex differences in eating disorder risk during puberty (i.e., higher rates in girls relative to boys) may be due to the protective effects of prenatal testosterone in boys and the "risky" effects of ovarian hormones in girls (Culbert et al., submitted).

Additional studies are also needed to identify the specific neurobiological systems that may be activated and/or organized by estrogen during puberty. Emerging data show strong phenotypic and genetic effects of estrogen on the pattern and timing of changes in brain structure and function during puberty (Ahmed et al., 2008; Nunez et al., 2002; Peper et al., 2009a; Peper et al., 2009b; Primus and Kellogg, 1991; Spear, 2000; Zehr et al., 2006). Yet, none of these studies have linked these changes to eating disorders or their symptoms. Several of the neurobiological systems that are regulated by estrogen and have been implicated in the etiology of eating disorders would be ideal targets for such investigations (Hildebrandt et al., 2010; Ostlund et al., 2003; Young, 2010). For example, estrogen regulates gene transcription within the serotonin system (Hildebrandt et al., 2010; Ostlund et al., 2003) including the serotonin 2a receptor and serotonin transporter, which have been

associated with AN and BN in neuroimaging and genetic research (Hildebrandt et al., 2010; Kaye, 2008; Klump and Culbert, 2007; Ostlund et al., 2003). Estrogen also regulates the production of BDNF (Schafman and MacLusky, 2008; Sohrabji et al., 1995; Solum and Handa, 2002; Toran-Allerand, 1996) which shows consistent genetic associations with eating disorders (Klump and Culbert, 2007; Rask-Andersen et al., 2010). Estrogen plays a highly significant role in the regulation of brain reward systems (Becker, 2009; Craft, 2008), including dopamine and opioids, consistently linked to preferences for the palatable and sweet foods ingested during binges in humans and animals (Berridge, 2009). Notably, many of these systems experience significant changes/maturation during the pubertal period (Becker, 2009; Friemel et al., 2010; Iughetti et al., 2011) that may be linked to estrogen (Becker, 2009) and may contribute to increases in pubertal risk. Human and animal studies examining whether estrogen regulation of these systems accounts for increased risk are needed to confirm a role for estrogen in pubertal increases in eating disorders.

Finally, studies that integrate across multiple levels of risk factors are needed to address traditional and emerging theories of eating disorder development during puberty. Similar to other behavioral phenotypes, eating disorders are unlikely to be caused by one type of risk factor, particularly since the same factor can impact risk via both biological and environmental processes. As an example, in the Harden et al. (2012) twin study discussed above, subjectively rated pubertal timing (i.e., whether the twin thought her development was earlier than her peers) was environmentally associated with increased risk for dieting in girls. This was in stark contrast to the findings for objectively measured pubertal timing (i.e., comparison of the twin's actual pubertal development to population norms) that was associated with increased dieting through genetic factors. The possibility that pubertal timing may be differentially associated with eating disorder risk depending upon the measurement/perspective underscores the strong need for multi-method, multi-level studies that examine biological and psychosocial risk factors and their interplay in the progression of eating disorder symptoms across development. These types of studies are likely to have the strongest impact on etiologic models as well as the eventual development of prevention programs that target the specific aspects of pubertal development (e.g., perception of timing) most amenable to change and psychosocial intervention.

Acknowledgments

This research was supported by a grant from the National Institute of Mental Health awarded to Dr. Klump (MH 070542). The content is solely the responsibility of the author and does not necessarily represent the official views of the NIMH.

References

- Abraham S, O'Dea JA. Body mass index, menarche, and perception of dieting among peripubertal adolescent females. *Int J Eat Disord.* 2001; 29:23–28. [PubMed: 11135329]
- Ackard DM, Peterson CB. Association between puberty and disordered eating, body image, and other psychological variables. *Int J Eat Disord.* 2001; 29:187–194. [PubMed: 11429981]
- Ahmed EI, Zehr JL, Schulz KM, Lorenz BH, DonCarlos LL, Sisk CL. Pubertal hormones modulate the addition of new cells to sexually dimorphic brain regions. *Nature Neuroscience.* 2008; 11:995–997.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 4. American Psychiatric Association; Washington, D.C: 2000. Text Revision (DSM-IV-TR)
- Aoki C, Sabaliauskas N, Chowdhury T, Min JY, Colacino AR, Laurino K, Barbarich-Marsteller NC. Adolescent female rates exhibiting activity-based anorexia express elevated levels of GABA_A Receptor $\alpha 4$ and δ subunits at the plasma membrane of hippocampal CA1 spines. *Synapse.* 2012; 66:391–407. [PubMed: 22213233]
- Asarian L, Geary N. Modulation of appetite by gonadal steroid hormones. *Philos Trans R Soc Lond B Biol Sci.* 2006; 361:1251–1263. [PubMed: 16815802]

- Attie I, Brooks-Gunn J. Development of eating problems in adolescent girls: A longitudinal study. *Dev Psychol.* 1989; 25:70–79.
- Babbs RK, Wojnicki FH, Corwin RL. Effect of 2-hydroxyestradiol on binge intake in rats. *Physiol Behav.* 2011; 103:508–512. [PubMed: 21497615]
- Baker JH, Thornton LM, Bulik CM, Kendler KS, Lichtenstein P. Shared genetic effects between age at menarche and disordered eating. *J Adolesc Health.* in press.
- Baker JH, Thornton LM, Lichtenstein P, Bulik CM. Pubertal development predicts eating behaviors in adolescence. *Int J Eat Disord.* 2012; 45:819–831. [PubMed: 22522282]
- Barker ET, Galambos NL. Body dissatisfaction of adolescent girls and boys: Risk and resource factors. *Journal of Early Adolescence.* 2003; 23:141–165.
- Becker JB. Sexual differentiation of motivation: A novel mechanism? *Horm Behav.* 2009; 55:646–654. [PubMed: 19446081]
- Bell DD, Zucker I. Sex differences in body weight and eating: Organization and activation by gonadal hormones in the rat. *Physiol Behav.* 1971; 7:27–34. [PubMed: 5149713]
- Berger U, Weitkamp K, Strauss B. Weight limits, estimations of future BMI, subjective pubertal timing and physical appearance comparisons among adolescent girls as precursors of disturbed eating behaviour in a community sample. *European Eating Disorders Review.* 2009; 17:128–136. [PubMed: 18729129]
- Berridge KC. 'Liking' and 'wanting' food rewards: Brain substrates and roles in eating disorders. *Physiol Behav.* 2009; 97:537–550. [PubMed: 19336238]
- Biederman J, Ball SW, Monuteaux MC, Surman CB, Johnson JL, Zeitlin S. Are girls with ADHD at risk for eating disorders? Results from a controlled, five-year prospective study. *Int J Eat Disord.* 2007; 40:232–240. [PubMed: 17262813]
- Blyth DA, Simmons RG, Zakin DF. Satisfaction with body image for early adolescent females: The impact of pubertal timing within different school environments. *Journal of Youth and Adolescence.* 1985; 14:207–225.
- Boggiano MM, Artiga AI, Pritchett CE, Chandler-Laney PC, Smith ML, Eldridge AJ. High intake of palatable food predicts binge-eating independent of susceptibility to obesity: an animal model of lean vs. obese binge-eating and obesity with and without binge-eating. *Int J Obes.* 2007; 31:1357–1367.
- Brooks-Gunn J, Rock D, Warren MP. Comparability of constructs across the adolescent years. *Dev Psychol.* 1989; 25:51–60.
- Brooks-Gunn J, Warren MP. The psychological significance of secondary sexual characteristics in nine- to eleven-year-old girls. *Child Dev.* 1988; 59:1061–1069. [PubMed: 3168614]
- Buffenstein R, Poppitt SD, McDevitt RM, Prentice AM. Food intake and the menstrual cycle: A retrospective analysis, with implications for appetite research. *Physiol Behav.* 1995; 58:1067–1077. [PubMed: 8623004]
- Bulik CM. Eating disorders in adolescents and young adults. *Child Adolesc Psychiatr Clin N Am.* 2002; 11:201–218. [PubMed: 12109318]
- Cattarin JA, Thompson JK. A three-year longitudinal study of body image, eating disturbance, and general psychological functioning in adolescent females. *Eating Disorders.* 1994; 2:114–125.
- Cauffman E, Steinberg L. Interactive effects of menarcheal status and dating on dieting and disordered eating among adolescent girls. *Dev Psychol.* 1996; 32:631–635.
- Combs JL, Pearson CM, Smith GT. A risk model for preadolescent disordered eating. *Int J Eat Disord.* 2011; 44:596–604. [PubMed: 21997422]
- Corcos M, Flament MF, Giraud MJ, Paterniti S, Ledoux S, Atger F, Jeammet P. Early psychopathological signs in bulimia nervosa. A retrospective comparison of the period of puberty in bulimic and control girls. *Eur Child Adolesc Psychiatry.* 2000; 9:115–121. [PubMed: 10926061]
- Cotrufo P, Cella S, Cremato F, Labella AG. Eating disorder attitude and abnormal eating behaviours in a sample of 11-13-year-old school children: The role of pubertal body transformation. *Eating and Weight Disorders.* 2007; 12:154–160. [PubMed: 18227636]
- Coughlin SS. Recall bias in epidemiologic studies. *J Clin Epidemiol.* 1989; 43:87–91. [PubMed: 2319285]

- Craft RM. Sex differences in analgesic, reinforcing, discriminative, and motoric effects of opioids. *Experimental and Clinical Psychopharmacology*. 2008; 16:376–385. [PubMed: 18837634]
- Crisp AH. Reported birth weights and growth rates in a group of patients with primary anorexia nervosa (weight phobia). *J Psychosom Res*. 1970; 14:23–50. [PubMed: 5441920]
- Culbert KM, Breedlove SM, Sisk CL, Burt SA, Klump KL. The emergence of sex differences in risk for disordered eating attitudes and behaviors during puberty: A role for prenatal testosterone exposure. *J Abnorm Psychol*. in press.
- Culbert KM, Burt SA, McGue M, Iacono WG, Klump KL. Puberty and the genetic diathesis of disordered eating attitudes and behaviors. *J Abnorm Psychol*. 2009; 118:788–796. [PubMed: 19899848]
- Cuthbert BN. Dimensional models of psychopathology: Research agenda and clinical utility. *J Abnorm Psychol*. 2005; 114:565–569. [PubMed: 16351380]
- de Castro JM, Goldstein SJ. Eating attitudes and behaviors of pre-and postpubertal females: Clues to the etiology of eating disorders. *Physiol Behav*. 1995; 58:15–23. [PubMed: 7667413]
- Domine F, Berchtold A, Akre C, Michaud PA, Suris JC. Disordered eating behaviors: What about boys? *J Adolesc Health*. 2009; 44:111–117. [PubMed: 19167658]
- Edler C, Lipson SF, Keel PK. Ovarian hormones and binge eating in bulimia nervosa. *Psychol Med*. 2007; 37:131–141. [PubMed: 17038206]
- Fabian LJ, Thompson JK. Body image and eating disturbance in young females. *Int J Eat Disord*. 1989; 8:63–74.
- Fairburn CG, Bohn K. Eating disorder NOS (EDNOS): An example of the troublesome "Not Otherwise Specified" (NOS) category in DSM-IV. *Behav Res Ther*. 2005; 43:691–701. [PubMed: 15890163]
- Fairburn CG, Cooper Z, Doll HA, Welch SL. Risk factors for anorexia nervosa: Three integrated case-control comparisons. *Arch Gen Psychiatry*. 1999; 56:468–476. [PubMed: 10232302]
- Fairburn CG, Welch SL, Doll HA, Davies BA, O'Connor ME. Risk factors for bulimia nervosa: A community-based case-control study. *Arch Gen Psychiatry*. 1997; 54:509–517. [PubMed: 9193191]
- Favaro A, Caregaro L, Tenconi E, Bosello R, Santonastaso P. Time trends in age at onset of anorexia nervosa and bulimia nervosa. *J Clin Psychiatry*. 2009; 70:1715–1721. [PubMed: 20141711]
- Favaro A, Ferrara S, Santonastaso P. The spectrum of eating disorders in young women: A prevalence study in a general population sample. *Psychosom Med*. 2003; 65:701–708. [PubMed: 12883125]
- Field AE, Camargo CA, Taylor CB, Berkey CS, Colditz A. Relation of peer and media influences to the development of purging behaviors among preadolescent and adolescent girls. *Archives of Pediatric and Adolescent Medicine*. 1999a; 153:1184–1189.
- Field AE, Camargo CA, Taylor CB, Berkey CS, Frazier AL, Gillman MW, Colditz GA. Overweight, weight concerns, and bulimic behaviors among girls and boys. *J Am Acad Child Adolesc Psychiatry*. 1999b; 38:754–760. [PubMed: 10361795]
- Folk L, Pedersen J, Cullari S. Body satisfaction and self-concept of third- and sixth-grade students. *Percept Mot Skills*. 1993; 76:547–553. [PubMed: 8483665]
- Fonesca H, Matos MG. Are adolescent weight-related problems and general well-being essentially an issue of age, gender or rather a pubertal timing issue? *J Pediatr Endocrinol Metab*. 2011; 24:251–256. [PubMed: 21823519]
- Fornari V, Dancyger IF. Psychosexual development and eating disorders. *Adolesc Med*. 2003; 14:61–75. [PubMed: 12529191]
- Friemel CM, Spanagel R, Schneider M. Reward sensitivity for a palatable food reward peaks during pubertal developmental in rats. *Frontiers in Behavioral Neuroscience*. 2010; 4:1–10. [PubMed: 20126432]
- Gagne DA, van Holle A, Brownley KA, Runfola CD, Hofmeier S, Branch KE, Bulik CM. Eating disorder symptoms and weight and shape concerns in a large web-based convenience sample of women ages 50 and above: Results of the gender and body image (GABI) study. *Int J Eat Disord*. 2012; 45:832–844. [PubMed: 22729743]
- Gentry RT, Wade GN. Sex differences in sensitivity of food intake, body weight, and running-wheel activity to ovarian steroids in rats. *J Comp Physiol Psychol*. 1976; 90:747–754. [PubMed: 965523]

- Graber JA, Brooks-Gunn J, Paikoff RL, Warren MP. Prediction of eating problems: An 8-year study of adolescent girls. *Dev Psychol.* 1994; 30:823–834.
- Graber JA, Lewinsohn PM, Seeley JR, Brooks-Gunn J. Is psychopathology associated with the timing of pubertal development? *J Am Acad Child Adolesc Psychiatry.* 1997; 36:1768–1776. [PubMed: 9401339]
- Gralen SJ, Levine MP, Smolak L, Murnen SK. Dieting and disordered eating during early and middle adolescence: Do the influences remain the same? *Int J Eat Disord.* 1990; 9:501–512.
- Harden KP, Mendle J, Kretsch N. Environmental and genetic pathways between early pubertal timing and dieting in adolescence: Distinguishing between objective and subjective timing. *Psychol Med.* 2012; 42:183–193. [PubMed: 21676282]
- Hayward C, Killen JD, Wilson DM, Hammer LD, Litt LF, Kraemer HC, Haydel F, Varady A, Taylor CB. Psychiatric risk associated with early puberty in adolescent girls. *J Am Acad Child Adolesc Psychiatry.* 1997; 36:255–262. [PubMed: 9031579]
- Hermes SF, Keel PK. The influence of puberty and ethnicity on awareness and internalization of the thin ideal. *Int J Eat Disord.* 2003; 33:465–467. [PubMed: 12658676]
- Hildebrandt T, Alfano L, Tricamo M, Pfaff DW. Conceptualizing the role of estrogens and serotonin in the development and maintenance of bulimia nervosa. *Clin Psychol Rev.* 2010; 30:655–668. [PubMed: 20554102]
- Hudson JI, Hiripi E, Pope HG, Kessler RC. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biol Psychiatry.* 2007; 61:348–358. [PubMed: 16815322]
- Iughetti L, Casarosa E, Predieri B, Patianna V, Luisi S. Plasma brain-derived neurotrophic factors in children and adolescents. *Neuropeptides.* 2011; 45:205–211. [PubMed: 21420165]
- Jacobi C, Hayward C, de Zwaan M, Kraemer HC, Agras WS. Coming to terms with risk factors for eating disorders: application of risk terminology and suggestions for a general taxonomy. *Psychol Bull.* 2004; 130:19–65. [PubMed: 14717649]
- Jaszyna-Gasior M, Schroeder JR, Thorner ED, Heishman SJ, Collins CC, Lo S, Moolchan ET. Age at menarche and weight concerns in relation to smoking trajectory and dependence among adolescent girls enrolled in a smoking cessation trial. *Addict Behav.* 2009; 34:92–95. [PubMed: 18940275]
- Johansson T, Ritzen EM. Very long-term follow-up of girls with early and late menarche. *Endocrine Development.* 2005; 8:126–136. [PubMed: 15722621]
- Johnson-Sabine E, Wood K, Patton G, Mann A, Wakeling A. Abnormal eating attitudes in London schoolgirls - a prospective epidemiological study: Factors associated with abnormal response on screening questionnaires. *Psychol Med.* 1988; 18:615–622. [PubMed: 3186865]
- Kaltiala-Heino R, Marttunen M, Rantanen P, Rimpela M. Early puberty is associated with mental health problems in middle adolescence. *Soc Sci Med.* 2003; 57:1055–1064. [PubMed: 12878105]
- Kaltiala-Heino R, Rimpela M, Rissanen A, Rantanen P. Early puberty and early sexual activity are associated with bulimic-type eating pathology in middle adolescence. *J Adolesc Health.* 2001; 28:346–352. [PubMed: 11287254]
- Kaltiala-Heino R, Rissanen A, Rimpela M, Rantanen P. Bulimia and bulimic behaviour in middle adolescence: More common than thought? *Acta Psychiatr Scand.* 1999; 100:33–39. [PubMed: 10442437]
- Kaluski DN, Natamba BK, Goldsmith R, Shimony T, Berry EM. Determinants of disordered eating behaviors among Israeli adolescent girls. *Eating Disorders.* 2008; 16:146–159. [PubMed: 18307114]
- Kaye W. Neurobiology of anorexia and bulimia nervosa. *Physiol Behav.* 2008; 94:121–135. [PubMed: 18164737]
- Keel PK, Fulkerson JA, Leon GR. Disordered eating precursors in pre- and early adolescent girls and boys. *Journal of Youth and Adolescence.* 1997; 26:203–216.
- Kendler KS, Aggen SH, Knudsen GP, Roysamb E, Neale MC, Reichborn-Kjennerud T. The structure of genetic and environmental risk factors for syndromal and subsyndromal common DSM-IV Axis I and all Axis II disorders. *A J Psychiatry.* 2010; 168:29–39.
- Keski-Rahkonen A, Bulik CM, Neale M, Rose RJ, Rissanen A, Kaprio J. Body dissatisfaction and drive for thinness in young adult twins. *Int J Eat Disord.* 2005; 37:188–199. [PubMed: 15822080]

- Killen J, Hayward C, Litt I, Hammer LD, Wilson DM, Miner B, Taylor CB, Varady A, Shisslak C. Is puberty a risk factor for eating disorders? *American Journal of Disorders of Childhood*. 1992; 146:323–325.
- Killen JD, Taylor CB, Wilson DM, Haydel KF, Hammer LD, Simmonds B, Robinson TN, Litt I, Varady A, Kraemer H. Pursuit of thinness and onset of eating disorder symptoms in a community sample of adolescent girls: A three-year prospective analysis. *Int J Eat Disord*. 1994; 16:227–238. [PubMed: 7833956]
- Klump KL, Burt SA, McGue M, Iacono WG. Changes in genetic and environmental influences on disordered eating across adolescence: A longitudinal twin study. *Arch Gen Psychiatry*. 2007a; 64:1409–1415. [PubMed: 18056549]
- Klump KL, Burt SA, McGue M, Iacono WG, Wade TM. Age differences in genetic and environmental influences on weight and shape concerns. *Int J Eat Disord*. 2010a; 43:679–688. [PubMed: 19950189]
- Klump KL, Culbert KM. Molecular genetic studies of eating disorders: Current status and future directions. *Current Directions in Psychological Science*. 2007; 16:37–41. [PubMed: 20539827]
- Klump KL, Culbert KM, Edler C, Keel PK. Ovarian hormones and binge eating: Exploring associations in community samples. *Psychol Med*. 2008; 38:1749–1757. [PubMed: 18307829]
- Klump KL, Culbert KM, Slane JD, Burt SA, Sisk CL, Nigg JT. The effects of puberty on genetic risk for disordered eating: Evidence for sex difference. *Psychol Med*. 2012; 42:627–638. [PubMed: 21854699]
- Klump KL, Gobrogge KL. A review and primer of molecular genetic studies of anorexia nervosa. *Int J Eat Disord*. 2005; 37:S43–S48. [PubMed: 15852319]
- Klump KL, Keel PK, Racine SE, Burt SA, Neale M, Sisk CL, Boker S, Hu JY. The interactive effects of estrogen and progesterone on changes in emotional eating across the menstrual cycle. *J Abnorm Psychol*. 2013; 122:131–137. [PubMed: 22889242]
- Klump KL, Keel PK, Sisk CL, Burt SA. Preliminary evidence that estradiol moderates genetic influences on disordered eating attitudes and behaviors during puberty. *Psychol Med*. 2010b; 40:1745–1753. [PubMed: 20059800]
- Klump KL, McGue M, Iacono WG. Age differences in genetic and environmental influences on eating attitudes and behaviors in female adolescent twins. *J Abnorm Psychol*. 2000; 109:239–251. [PubMed: 10895562]
- Klump KL, McGue M, Iacono WG. Differential heritability of eating attitudes and behaviors in prepubertal versus pubertal twins. *Int J Eat Disord*. 2003; 33:287–292. [PubMed: 12655625]
- Klump KL, Perkins P, Burt SA, McGue M, Iacono WG. Puberty moderates genetic influences on disordered eating. *Psychol Med*. 2007b; 37:627–634. [PubMed: 17335640]
- Klump KL, Suisman JL, Culbert KM, Kashy DA, Keel PK, Sisk CL. The effects of ovariectomy on binge eating proneness in adult female rats. *Horm Behav*. 2011a; 59:585–593. [PubMed: 21376721]
- Klump KL, Suisman JL, Culbert KM, Kashy DA, Sisk CL. Binge eating proneness emerges during puberty in female rats: A longitudinal study. *J Abnorm Psychol*. 2011b; 120:948–955. [PubMed: 21574664]
- Koff E, Rierdan J. Advanced pubertal development and eating disturbance in early adolescent girls. *The Journal of Adolescent Health*. 1993; 14:433–439. [PubMed: 8241198]
- Krueger RF, Markon KE. A dimensional-spectrum model of psychopathology: Progress and opportunities. *Arch Gen Psychiatry*. 2011; 68:10–11. [PubMed: 21199961]
- Lantzouni E, Frank GR, Golden NH, Shenker RI. Reversibility of growth stunting in early onset anorexia nervosa: A prospective study. *The Journal of Adolescent Health*. 2002; 31:162–165. [PubMed: 12127386]
- Leon GR, Fulkerson JA, Perry CL, Cudeck R. Personality and behavioral vulnerabilities associated with risk status for eating disorders in adolescent girls. *J Abnorm Psychol*. 1993; 102:438–444. [PubMed: 8408956]
- Leon GR, Fulkerson JA, Perry CL, Early-Zald MB. Prospective analysis of personality and behavioral vulnerabilities and gender influences in the later development of disordered eating. *J Abnorm Psychol*. 1995; 104:140–149. [PubMed: 7897036]

- Levine MP, Smolak L, Moodey AF, Shuman MD, Hessen LD. Normative developmental challenges and dieting and eating disturbances in middle school girls. *Int J Eat Disord.* 1994; 15:11–20. [PubMed: 8124323]
- Machado PP, Machado BC, Goncalves S, Hoek HW. The prevalence of eating disorders not otherwise specified. *Int J Eat Disord.* 2007; 40:212–217. [PubMed: 17173324]
- Mangweth-Matzek B, Rupp CI, Hausmann A, Kemmler G, Biebl W. Menarche, puberty and first sexual activities in eating-disordered patients as compared with a psychiatric and a nonpsychiatric control group. *Int J Eat Disord.* 2007; 40:705–710. [PubMed: 17610254]
- McCabe MP, Ricciardelli LA. A longitudinal study of pubertal timing and extreme body change behaviors among adolescent boys and girls. *Adolescence.* 2004; 39:145–166. [PubMed: 15230071]
- McCabe MP, Ricciardelli LA, Banfield S. Body image, strategies to change muscles and weight, and puberty: Do they impact on positive and negative affect among adolescent boys and girls? *Eating Behaviors.* 2001; 2:129–149. [PubMed: 15001042]
- McCabe MP, Ricciardelli LA, Finemore J. The role of puberty, media and popularity with peers on strategies to increase weight, decrease weight and increase muscle tone among adolescent boys and girls. *J Psychosom Res.* 2002; 52:145–153. [PubMed: 11897233]
- McHale SM, Corneal DA, Crouter AC, Birch LL. Gender and weight concerns in early and middle adolescence: Links with well-being and family characteristics. *J Clin Child Psychol.* 2001; 30:338–348. [PubMed: 11501251]
- Michaud PA, Suris JC, Deppen A. Gender-related psychological and behavioural correlates of pubertal timing in a national sample of Swiss adolescents. *Mol Cell Endocrinol.* 2006; 254–255. 172–178.
- Mousa TY, Al-Domi HA, Mashal RH, Jibril MAK. Eating disturbances among adolescent schoolgirls in Jordan. *Appetite.* 2010; 54:196–201. [PubMed: 19900499]
- Muris P, Meesters C, van de Blom W, Mayer B. Biological, psychological, and sociocultural correlates of body change strategies and eating problems in adolescent boys and girls. *Eating Behaviors.* 2005; 6:11–22. [PubMed: 15567107]
- Nicholls DE, Viner RM. Childhood risk factors for lifetime anorexia nervosa by age 30 years in a national birth cohort. *J Am Acad Child Adolesc Psychiatry.* 2009; 48:791–799. [PubMed: 19564797]
- Nielsen S. Evaluation of growth in anorexia nervosa from serial measurements. *J Psychiatr Res.* 1985; 19:227–230. [PubMed: 4045740]
- Niven AG, Fawcner SG, Knowles AM, Stephenson C. Maturation differences in physical self-perceptions and the relationship with physical activity in early adolescent girls. *Pediatric Exercise Science.* 2007; 19:472–480. [PubMed: 18089913]
- Nottelmann ED, Susman RN, Inoff-Germain G, Cutler GB, Loriaux MD, Chrousos GP. Developmental processes in early adolescence: Relationships between adolescent adjustment problems and chronologic age, pubertal stage, and puberty-related serum hormone levels. *Adolesc Med.* 1986; 110:473–480.
- Nunez JL, Sodhi J, Juraska JM. Ovarian hormones after postnatal day 20 reduce neuron number in the rat primary visual cortex. *Journal of Neurobiology.* 2002; 52:312–321. [PubMed: 12210098]
- O'Dea JA, Abraham S. Onset of disordered eating attitudes and behaviors in early adolescence: Interplay of pubertal status, gender, weight, and age. *Adolescence.* 1999a; 34:671–679. [PubMed: 10730692]
- O'Dea JA, Abraham S. Association between self-concept and body weight, gender, and pubertal development among male and female adolescents. *Adolescence.* 1999b; 34:69–79. [PubMed: 10234368]
- Ohring R, Graber JA, Brooks-Gunn J. Girls' recurrent and concurrent body dissatisfaction: Correlates and consequences over 8 years. *Int J Eat Disord.* 2002; 31:404–415. [PubMed: 11948645]
- Oinonen KA, Bird JL. Age at menarche and digit ratio (2D:4D): Relationships with body dissatisfaction, drive for thinness, and bulimia symptoms in women. *Body Image.* 2012; 9:302–306. [PubMed: 22245563]

- Ostlund H, Keller E, Hurd YL. Estrogen receptor gene expression in relation to neuropsychiatric disorders. *Annals of the New York Academy of Sciences*. 2003; 1007:54–63. [PubMed: 14993040]
- Patel BP, Bellissimo N, Thomas SG, Hamilton JK, Anderson GH. Television viewing at mealtime reduces caloric compensation in peripubertal, but not postpubertal, girls. *Pediatr Res*. 2011; 70:513–517. [PubMed: 21772226]
- Pearson CM, Combs JL, Smith GT. A risk model for disordered eating late elementary school boys. *Psychology of Addictive Behaviors*. 2010; 24:696–704.
- Peper JS, Brouwer RM, Schnack HG, van Baal GC, van Leeuwen M, van den Berg SM, Delemarre-Van de Waal HA, Boomsma DI, Kahn RS, Hulshoff Pol HE. Sex steroids and brain structure in pubertal boys and girls. *Psychoneuroendocrinology*. 2009a; 34:332–342. [PubMed: 18980810]
- Peper JS, Schnack HG, Brouwer RM, Van Baal GC, Pjetri E, Szekely E, Van Leeuwen M, Van den Berg SM, Collins DL, Evans AC, Boomsma DI, Kahn RS, Hulshoff Pol HE. Heritability of regional and global brain structure at the onset of puberty: A magnetic resonance imaging study in 9-year-old twin pairs. *Human Brain Mapping*. 2009b; 30:2184–2196. [PubMed: 19294640]
- Petersen AC, Leffert N, Graham B, Ding S, Overbey T. Depression and body image disorders in adolescence. *Womens Health Issues*. 1994; 4:98–108. [PubMed: 8086824]
- Primus RJ, Kellogg CK. Gonadal status and pubertal age influence the responsiveness of the benzodiazepine/GABA receptor complex to environmental challenge in male rats. *Brain Research*. 1991; 561:299–306. [PubMed: 1666328]
- Racine SE, Culbert KM, Keel PK, Sisk CL, Burt SA, Klump KL. Differential associations between ovarian hormones and disordered eating symptoms across the menstrual cycle in women. *Int J Eat Disord*. 2012; 45:333–344. [PubMed: 21656540]
- Rask-Andersen M, Olszewski PK, Levine AS, Schiöth HB. Molecular mechanisms underlying anorexia nervosa: Focus on human gene association studies and systems controlling food intake. *Brain Res*. 2010; 62:147–164.
- Reichborn-Kjennerud T, Bulik CM, Sullivan PF, Tambs K, Harris JR. Psychiatric and medical symptoms in binge eating in the absence of compensatory behaviors. *Obes Res*. 2004; 12:1445–1454. [PubMed: 15483209]
- Ricciardelli LA, McCabe MP. A longitudinal analysis of the role of biopsychosocial factors in predicting body change strategies among adolescent boys. *Sex Roles*. 2003; 48:349–359.
- Rodriguez-Tome H, Bariaud F, Zardi MF, Delmas C, Jeanvoine B, Szylagyi P. The effects of pubertal changes on body image and relations with peers of the opposite sex in adolescence. *J Adolesc*. 1993; 16:421–438. [PubMed: 8138609]
- Romans SE, Gendall KA, Martin JL, Mullen PE. Child sexual abuse and later disordered eating: A New Zealand epidemiological study. *Int J Eat Disord*. 2001; 29:380–392. [PubMed: 11285575]
- Root TL, Szatkiewicz JP, Jonassaint CR, Thornton LM, Pinheiro AP, Strober M, Bloss C, Berrettini W, Schork NJ, Kaye WH, Bergen AW, Magistretti P, Brandt H, Crawford S, Crow S, Fichter MM, Goldman D, Halmi KA, Johnson C, Kaplan AS, Keel PK, Klump KL, La Via M, Mitchell JE, Rotondo A, Treasure J, Woodside DB, Bulik CM. Association of candidate genes with phenotypic traits relevant to anorexia nervosa. *European Eating Disorders Review*. 2011; 19:487–493. [PubMed: 21780254]
- Rowe R, Pickles A, Simonoff E, Bulik CM, Silberg JL. Bulimic symptoms in the Virginia Twin Study of Adolescent Behavioral Development: Correlates, comorbidity, and genetics. *Biol Psychiatry*. 2002; 51:172–182. [PubMed: 11822996]
- Roze C, Doyen C, Le Heuzey MF, Armoogum P, Mouren MC, Leger J. Predictors of late menarche and adult height in children with anorexia nervosa. *Clin Endocrinol (Oxf)*. 2007; 67:462–467. [PubMed: 17561975]
- Ruuska J, Kaltiala-Heino R, Koivisto AM, Rantanen P. Puberty, sexual development and eating disorders in adolescent outpatients. *Eur Child Adolesc Psychiatry*. 2003; 12:214–220. [PubMed: 14667108]
- Schafman HE, MacLusky NJ. Estrogen-growth factor interactions and their contributions to neurological disorders. *Headache*. 2008; 48:S77–S89. [PubMed: 18700946]

- Shisslak CM, Crago M, McKnight KM, Estes LS, Gray N, Parnaby OG. Potential risk factors associated with weight control behaviors in elementary and middle school girls. *J Psychosom Res.* 1998; 44:301–313. [PubMed: 9587875]
- Siegel JM, Yancey AK, Aneshensel CS, Schuler R. Body image, perceived pubertal timing, and adolescent mental health. *The Journal of Adolescent Health.* 1999; 25:155–165. [PubMed: 10447043]
- Silberg JL, Bulik CM. The developmental association between eating disorder symptoms and symptoms of depression and anxiety in juvenile twin girls. *J Child Psychol Psychiatry.* 2005; 46:1317–1326. [PubMed: 16313432]
- Sisk CL, Zehr JL. Pubertal hormones organize the adolescent brain and behavior. *Front Neuroendocrinol.* 2005; 26:163–174. [PubMed: 16309736]
- Slap GB, Khalid N, Paikoff RL, Brooks-Gunn J, Warren MP. Evolving self-image, pubertal manifestations, and pubertal hormones: Preliminary findings in young adolescent girls. *J Adolesc Health.* 1994; 15:327–335. [PubMed: 7918506]
- Smolak L, Stein JA. The relationship of drive for muscularity to sociocultural factors, self-esteem, physical attributes gender role, and social comparison in middle school boys. *Body Image.* 2006; 3:121–129. [PubMed: 18089215]
- Sohrabji F, Miranda RC, Toran-Allerand CD. Identification of a putative estrogen response element in the gene encoding brain-derived neurotrophic factor. *Proc Natl Acad Sci U S A.* 1995; 92:11110–11114. [PubMed: 7479947]
- Solum DT, Handa RJ. Estrogen regulates the development of brain-derived neurotrophic factor mRNA and protein in the rat hippocampus. *J Neurosci.* 2002; 22:2650–2659. [PubMed: 11923430]
- Spear LP. The adolescent brain and age-related behavioral manifestations. *Neuroscience and Biobehavioral Reviews.* 2000; 24:417–463. [PubMed: 10817843]
- Stice E, Presnell K, Bearman SK. Relation of early menarche to depression, eating disorders, substance abuse, and comorbid psychopathology among adolescent girls. *Dev Psychol.* 2001; 37:608–619. [PubMed: 11552757]
- Stormer SM, Thompson JK. Explanations of body image disturbance: A test of maturational status, negative verbal commentary, social comparison, and sociocultural hypotheses. *Int J Eat Disord.* 1996; 19:193–202. [PubMed: 8932558]
- Striegel-Moore RH, McMahon RP, Biro FM, Schreiber G, Crawford PB, Voorhees C. Exploring the relationship between timing of menarche and eating disorder symptoms in black and white adolescent girls. *Int J Eat Disord.* 2001; 30:421–433. [PubMed: 11746303]
- Suka M, Sugimori H, Yoshida K, Kanayama H, Sekine M, Yamagami T, Kagamimori S. Body image and body satisfaction play important roles in the path to dieting behavior in Japanese preadolescents: The Toyama birth cohort study. *Environmental Health and Preventive Medicine.* 2005; 10:324–330. [PubMed: 21432115]
- Swithers SE, McCurley M, Hamilton EAD. Influence of ovarian hormones on development of ingestive responding to alterations in fatty acid oxidation in female rats. *Horm Behav.* 2008; 54:471–477. [PubMed: 18586247]
- Tenconi E, Lunardi N, Zanetti T, Santonastaso P, Favaro A. Predictors of binge eating in restrictive anorexia nervosa patients in Italy. *The Journal of Nervous and Mental Disease.* 2006; 194:712–715. [PubMed: 16971825]
- The McKnight Investigators. Risk factors for the onset of eating disorders in adolescent girls: Results of the McKnight longitudinal risk factor study. *Am J Psychiatry.* 2003; 160:248–254. [PubMed: 12562570]
- Thomas JJ, Vartanian LR, Brownell KD. The relationship between eating disorder not otherwise specified (EDNOS) and officially recognized eating disorders: Meta-analysis and implications for DSM. *Psychol Bull.* 2009; 135:407–433. [PubMed: 19379023]
- Thompson AM, Chad KE. The relationship of pubertal status to body image, social physique anxiety, preoccupation with weight and nutritional status in young females. *Can J Public Health.* 2000; 91:207–211. [PubMed: 10927850]

- Toran-Allerand CD. Mechanisms of estrogen action during neural development: mediation by interactions with the neurotrophins and their receptors? *J Steroid Biochem Mol Biol.* 1996; 56:169–178. [PubMed: 8603038]
- Tremblay L, Lariviere M. The influence of puberty onset, body mass index, and pressure to be thin on disordered eating behaviors in children and adolescents. *Eating Behaviors.* 2009; 10:75–83. [PubMed: 19447348]
- Wade, GN. Sex hormones, regulatory behaviors, and body weight. In: Rosenblatt, JS.; Hinde, RA.; Shaw, E., editors. *Advances in the Study of Behavior.* Academic Press, Inc; New York: 1976. p. 201-279.
- Walsh BT. Eating disorders in DSM-V: Review of existing literature (Part 1). *Int J Eat Disord.* 2009; 42:579–580. [PubMed: 19718671]
- Warren MP, Brooks-Gunn J. Mood and behavior at adolescence: Evidence for hormonal factors. *The Journal of Clinical Endocrinology and Metabolism.* 1989; 69:77–83. [PubMed: 2525135]
- Wichstrom L. Social, psychological, and physical correlates of eating problems. A study of the general adolescent population in Norway. *Psychol Med.* 1995; 25:567–579. [PubMed: 7480437]
- Wilson, JD.; Foster, DW.; Kronenberg, HM.; Larsen, PR. *Williams Textbook of Endocrinology.* 9. W.B. Saunders Company; Philadelphia, PA: 1998.
- Young JK. Anorexia nervosa and estrogen: Current status of the hypothesis. *Neurosci Biobehav Rev.* 2010; 34:1195–1200. [PubMed: 20138911]
- Yu Z, Geary N, Corwin RL. Ovarian hormones inhibit fat intake under binge-type conditions in ovariectomized rats. *Physiol Behav.* 2008; 95:501–507. [PubMed: 18706435]
- Zehr JL, Culbert KM, Sisk CL, Klump KL. An association of early puberty with disordered eating and anxiety in a population of undergraduate women and men. *Horm Behav.* 2007; 52:427–435. [PubMed: 17707381]
- Zehr JL, Todd BJ, Schulz KM, McCarthy MM, Sisk CL. Dendritic pruning of the medial amygdala during pubertal development of the male Syrian hamster. *Journal of Neurobiology.* 2006; 66:578–590. [PubMed: 16555234]

Research Highlights

- Human and animal studies of pubertal risk for eating disorders are reviewed.
- Advanced pubertal status and early pubertal timing increase risk in girls.
- Puberty is less consistently linked to eating disorder risk in boys.
- Female-specific risk may be due to estrogen activation of genetic influences.

Table 1

Definitions of DSM IV Diagnoses and Eating Disorder Symptoms that have been Investigated in Studies of Puberty.

Diagnoses/Symptoms	Definition
Diagnoses:	
Anorexia nervosa (AN)	<p>All of the following are present:</p> <ol style="list-style-type: none"> 1 Low body weight (i.e., < 85% of ideal for age and height). 2 Fear of becoming fat or of gaining weight. 3 Distortion in the way in which body weight and shape are perceived (i.e., thinks part(s) of body too fat, undue influence of body weight/shape on self-esteem, denial of seriousness of low body weight). 4 Primary amenorrhea or (in post-menarcheal females) loss of menses for 3 consecutive months.
Bulimia nervosa (BN)	<p>All of the following are present:</p> <ol style="list-style-type: none"> 1 Binge eating (i.e., the consumption of a large amount of food in short period of time (i.e., 2 hours) with a loss of control over the binge episode). 2 Use of inappropriate compensatory behaviors including purging (i.e., self-induced vomiting, or abuse of laxatives, diuretics, or enemas) and non-purging (e.g., excessive exercise, fasting) behaviors. 3 Binge eating and inappropriate compensatory behaviors occur, on average, 2 times per week for 3 months. 4 Undue influence of body weight and/or shape on self-esteem. 5 The BN symptoms do not occur exclusively during periods of AN.
Eating Disorder Not Otherwise Specified (EDNOS)	<p>Clinically significant syndromes that do not meet criteria for either AN or BN – examples include:</p> <ol style="list-style-type: none"> 1 A woman who would meet criteria for BN but who engages in binge eating/purging episodes only 1 time per week for 3 months. 2 A woman who would meet criteria for AN except that her body weight is 90% of ideal. 3 Binge eating disorder, i.e., a woman who binge eats but does not regularly engage in compensatory behaviors.
Symptoms:	
Body dissatisfaction, weight/shape concerns	Dissatisfaction with the size/shape of one's body or body parts, and/or preoccupation with weight and a desire to lose weight
Dieting/Weight management	Behavioral attempts to restrict food intake and/or engage in other behaviors to lose weight (e.g., exercise).
Dietary restraint	A cognitive intent to diet (i.e., desire to lose weight, plans to restrict food intake) as well as actual attempts to lose weight through dieting, avoidance of high fat foods, and/or fasting.
Binge eating	See definition above under BN
Purging behaviors	See definition above under BN
Drive for muscularity	Both an intent/desire to increase muscle mass as well as actual attempts to increase muscle mass (e.g., weight lifting, protein shakes).

Table 2

Summary of Studies Examining the Effects of Advanced Pubertal Status and Early Pubertal Timing on Eating Disorders and Their Symptoms.

Study	Advanced Pubertal Status		Early Pubertal Timing	
	Yes	No	Yes	No
<u>FEMALES</u>				
<u>Eating Disorder Diagnoses</u>				
<u>AN</u>				
Crisp (1970)			X	
Fairburn et al. (1999)				X
Favaro et al. (2003)				X
Nicholls and Viner (2009)			X ^a	
Nielsen (1985)				X
Mangweth-Matzek et al. (2007)				X
Ruuska et al. (2003)				X
Stice et al. (2001)				X
<u>BN</u>				
Corcos et al. (2000)			X	
Fairburn et al. (1997)			X	
Fairburn et al. (1999)			X	
Favaro et al. (2003)				X
Kaltiala-Heino et al. (1999)		X		
Kaltiala-Heino et al. (2001)			X	
Kaltiala-Heino et al. (2003)			X	
Killen et al. (1992)	X			
Killen et al. (1994)		X		
Mangweth-Matzek et al. (2007)				X
Mousa et al. (2010)	X			
Ruuska et al. (2003)			X	
Stice et al. (2001)				X
<u>AN and BN Combined</u>				
Biederman et al. (2007)	X			
Favaro et al. (2003)	X			
Graber et al. (1997)	X			
Romans et al. (2001)	X			
<u>EDNOS</u>				
Mousa et al. (2010)	X			
<u>Eating Disorder Symptoms</u>				
<u>Global Measures</u>				
Attie and Brooks-Gunn (1989)	X			

Study	Advanced Pubertal Status		Early Pubertal Timing	
	Yes	No	Yes	No
Baker et al. (2012)			X	
Baker et al. (in press)			X	
Berger et al. (2009)			X	
Culbert et al. (2009)	X			
Culbert et al. (submitted)	X			
Graber et al. (1994)			X	
Hayward et al. (1997)	X		X	
Johnson-Sabine et al. (1988)				X
Kaluski et al. (2008)			X	
Keel et al. (1997)	X			
Klump et al. (2003)	X			
Klump et al. (2007b)	X			
Leon et al. (1993)				X
Leon et al. (1995)				X
Levine et al. (1994)		X		
The McKnight Investigators (2003)		X		
Wichstrom (1995)			X	
<u>Body Dissatisfaction and Weight/Shape Concerns:</u>				
Ackard and Peterson (2001)			X	
Barker and Galambos (2003)		X		
Berger et al. (2009)	X			
Blyth et al. (1985)			X	
Brooks-Gunn et al. (1989)			X	
Cattarin and Thompson (1994)		X		
Cauffman and Steinberg (1996)	X			
Cotrufo et al. (2007)	X			
Culbert et al. (submitted)	X			
de Castro and Goldstein (1995)	X			
Fabian and Thompson (1989)	X			
Folk et al. (1993)		X		
Fonesca and Matos (2011)			X	
Hermes and Keel (2003)	X			
Jaszyna-Gasior et al. (2009)				X
Keski-Rahkonen et al. (2005)	X			
Koff and Rierdan (1993)	X			
Levine et al. (1994)		X		
McCabe et al. (2001)	X			
McCabe and Ricciardelli (2004)	X			
McHale et al. (2001)	X			
Michaud et al. (2006)	X			

Study	Advanced Pubertal Status		Early Pubertal Timing	
	Yes	No	Yes	No
Muris et al. (2005)		X		
Niven et al. (2007)	X			
Ohring et al. (2002)	X			
Oinonen and Bird (2012)	X			
O'Dea and Abraham (1999a)	X			
O'Dea and Abraham (1999b)	X			
Petersen et al. (1994)			X	
Rodriguez-Tome et al. (1993)		X		
Siegel et al. (1999)	X			
Stormer and Thompson (1996)				X
Striegel-Moore et al. (2001)			X	
Suka et al. (2005)	X			
Thompson and Chad (2000)	X			
Tremblay and Lariviere (2009)	X			
Zehr et al. (2007)			X	
<u>Dieting and Weight Management</u>				
Abraham and O'Dea (2001)	X			
Baker et al. (in press)	X			
Cotrufo et al. (2007)	X			
Field et al. (1999b)	X			
Gralen et al. (1990)	X			
Johansson and Ritzen (2005)			X	
Levine et al. (1994)	X			
McCabe et al. (2002)	X			
McCabe and Ricciardelli (2004)	X			
Harden et al. (2012)			X	
Shisslak et al. (1998)		X		
Tremblay & Lariviere (2009)	X			
<u>Dietary Restraint</u>				
de Castro & Goldstein (1995)	X			
Patel et al. (2011)	X			
Zehr et al. (2007)			X	
<u>Binge Eating</u>				
Cattarin & Thompson (1994)		X		
Combs et al. (2011)				
Cotrufo et al. (2007)	X			
Field et al. (1999b)	X			
Gralen et al. (1990)	X			
Koff & Rierdan (1993)		X		

Study	Advanced Pubertal Status		Early Pubertal Timing	
	Yes	No	Yes	No
McCabe & Ricciardelli (2004)				X
Reichborn-Kjennerud et al. (2004) (Reichborn- Kjennerud et al., 2004)			X	
Striegel-Moore et al. (2001)				X
Tenconi et al. (2006)			X	
Thompson and Chad (2000)	X			
<u>Purging</u>				
Combs et al. (2011)	X			
Field et al. (1999b)	X			
Field et al. (1999a)	X			
<u>MALES</u>				
<u>Eating Disorder Diagnoses</u>				
<u>AN</u>				
Nielsen (1985)			X	
<u>BN</u>				
Kaltialo-Heino (1999)		X		
Kaltialo-Heino (2003)			X	
<u>Eating Disorder Symptoms</u>				
<u>Global Measures</u>				
Baker et al. (in press)	X			
Cortufo et al. (2007)	X			
Culbert et al. (submitted)		X		
Domine et al. (2009)			X	
Keel et al. (1997)		X		
Leon et al. (1995)				X
Reichborn-Kjennurud et al. (2004)				X
<u>Body Dissatisfaction and Weight/Shape Concerns</u>				
Barker & Galambos (2003)		X		
Cortufo et al. (2007)	X			
Folk et al. (1993)	X			
Keski-Rahkonen et al. (2005)		X		
Michaud et al. (2006)			X	
McCabe et al. (2001)	X			
McHale et al. (2001)	X			
Siegel et al. (1999)			X	
Suka et al. (2005)	X			
Zehr et al. (2007)			X	
<u>Dieting and Weight Management</u>				

Study	Advanced Pubertal Status		Early Pubertal Timing	
	Yes	No	Yes	No
Baker et al. (in press)		X		
Cortufo et al. (2007)	X			
McCabe et al. (2002)	X			
McCabe & Ricciardelli (2004)			X	
Suka et al. (2005)	X			
<u>Dietary Restraint</u>				
Zehr et al. (2007)			X	
<u>Binge Eating</u>				
Cortufo et al. (2007)	X			
Pearson et al. (2010)		X		
Reichborn-Kjennerud et al. (2004)				X
Zehr et al. (2007)			X	
<u>Purging</u>				
Field et al. (1999b)	X			
Pearson et al. (2010)		X		
<u>Drive for Muscularity</u>				
McCabe & Ricciardelli (2004)	X			
Ricciardelli and McCabe (2003)		X		
Smolak and Stein (2006)		X		

Note. The “X” indicates whether the study did (yes) or did not (no) find a significant effect of advanced pubertal status or early pubertal timing on eating disorders/symptoms. Some studies included males and females in the same sample but did not examine them separately in analyses. In all of these cases, sex was a significant predictor of eating problems, with females being at significantly increased risk for eating pathology relative to males. Consequently, the results of these studies are included in table entries for females but not males.

^aEffect was trend-level ($p = .06$) and became non-significant when included in models that controlled for sex and socioeconomic status.