Puberty onset of gender differences in rates of depression: a developmental, epidemiologic and neuroendocrine perspective

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Summary

A dramatic feature of the epidemiology of depression is the appearance of a 2:1 female excess of depression during adolescence. In childhood, rates of depression either do not differ between boys and girls or show a slight excess in boys. In this paper we review a number of lines of evidence that implicate the physical and hormonal developments of puberty in this change. We also argue that the analysis of pubertal change in the etiology of depression must take into account the fact that the causation of depression is almost certainly a complex process. In understanding such a process we suggest that developmental epidemiological studies will be of particular value.

Key words: Depression; Adolescents; Puberty; Sex hormones

Introduction

One of the best replicated epidemiological findings in the psychiatric literature is that the prevalence of unipolar depression in women is about twice that found in men (Weissman and Klerman, 1977). However, studies of children have found either no gender differences in rates or a slight excess in boys. However by the age of 15 the female predominance is established (Guyer et al., 1989; Velez et al., 1989; McGee et al., 1990; Rutter et al., 1976; Anderson et al., 1987; Bird et al., 1988; Cohen and Brook, 1987; Kashani et al., 1987; Velez et al., 1989; McGee et al., 1990; McGee and Williams, 1988; Costello, unpublished data; Nolen-Hoeksema et al., 1991; Angold and Rutter, 1992; Costello and DeRosier, 1993). It is as yet uncertain whether the excess of depressed teenage girls is due solely to an increase in the rates of depression in girls or is also augmented by a decline in the rate of depression in teenage boys (Angold et al., 1993). A majority of studies indicate that gender-related differences are apparent by the age of 12 (and perhaps 2 or 3 years before that). There is also evidence that the rate of depression continues to rise in girls well beyond this age (see Angold and Rutter, 1992; Angold et al., 1993, for reviews). The change in
rates of depression therefore occurs at the same time as the hormonal and physical changes of puberty, and the many psychological, behavioral and social transitions that accompany them. This coincidence of timing has, not unnaturally, led to the suggestion that the physiological changes of puberty may be responsible in some way for the change in rates of depression. The purpose of this paper is to bring together several lines of research from child and adult psychopathology and endocrinology and to focus them on a research agenda for understanding the relationship between depression and the physiological changes of puberty, and to indicate the weaknesses in the literature to date.

**Age changes in patterns of depressive symptomatology**

Although sex-differentiated age trends in the prevalence of depression are clearly present, the patterns of symptomatology that contribute to those trends are less well explored. Unresolved issues include whether patterns of symptomatology shift over the course of puberty, and whether gender differences in those patterns first emerge at this time. Consideration of relevant findings should be prefaced by the recognition that, if the base rates of individual symptoms in the population change both with age and in relation to each other, then their relative weights in contributing to the diagnosis of depression may also change. As yet we are very short of data on such changes in relation to other symptoms of depression (Mascie-Taylor, 1991), but there is evidence that they occur and that such developmental progressions may need to be incorporated into current nosologies (Digdon and Gotlib, 1985). For instance, McConville et al. (1973) have described three forms of depression characterized by ‘affectual symptoms’, guilt, and low self-esteem respectively. The ‘affectual type’ was more common in 6 to 8 year-olds, while the low self-esteem type appeared with increasing frequency at later ages. The guilt type, which resembled adult psychotic depression, mostly emerged after the age of 11. Inamdar et al. (1979) noted the absence of motor agitation or retardation, delusions of guilt, and hopelessness in their sample of 30 depressed adolescents; though these symptoms have been reported in adolescents with depression (Strober et al., 1981; Chambers et al., 1982; Kazdin and Petti, 1982; Friedman et al., 1983a; Friedman et al., 1983b), they may be rarer in childhood and early adolescence than in adulthood.

Ryan et al. (1987) compared the symptomatology of 95 pre-pubertal children and 92 adolescents with Major Depressive Disorder, as assessed by the K-SADS interview (Chambers et al., 1985). The prepubertal children had more somatic complaints, psychomotor agitation, separation anxiety, phobias and hallucinations, and presented a more depressed appearance, while the adolescents suffered from more anhedonia, hopelessness, hypersonmia, weight change, use of illicit drugs, and lethality of suicide attempts (though not more severe suicidal ideation or intent). However, these represented only a minority of the symptoms evaluated, and they concluded that the similarities between the depressions of the younger and older groups were more striking than the differences. In contrast to the findings of Inamdar et al. (1979), psychomotor agitation and retardation and hopelessness were very common in both the children and adolescents.

Mitchell et al. (1988) compared the symptoms of 45 depressed children with those of 50 adolescents, interviewed with the K-SADS. They found only one significant difference in symptom rates; hypersonmia was commoner in the adolescents. But comparison with the rates of symptoms in young adult depressives reported earlier by Baker et al. (1971) revealed more extensive differences. The combined child and adolescent group had higher rates of guilt, somatic complaints, low self-esteem, suicidal attempts, and hallucinations, while the adults had higher rates of early morning waking, anorexia, weight loss, and delusions. However, there are a number of problems with this latter comparison. Mitchell et al.’s young patients were mostly outpatients, while the Baker et al. study looked at inpatient adults detected in 1971, and used different assessment instruments.

Weissman et al. (1987) found that older children with Major Depressive Disorder (MDD) more often reported weight loss and insomnia than younger depressed children. Angold et al. (1987) followed up this finding in a larger subset
of children from the same study of children at low and high familial risk of depression who met the Part A DSM-III (1980) criterion for Major Depressive Disorder. Symptom data were collected with the K-SADS-E. These analyses were therefore based on the reports of the 89 children who met this criterion, and the 62 parents who said that their children met this criterion. Episodes of depressed mood or anhedonia occurring in older girls were marked by considerably more sleep and appetite disturbance, and an increase in cognitive symptoms, concentration problems, and suicidality than those occurring in younger girls and boys of all ages. There was no change in the rates of symptoms defining melancholia. No such age effects appeared in the reports of either the boys or the parent reports about boys or girls.

A number of problems arise in trying to compare these sometimes divergent findings. All of Ryan et al.’s subjects had been referred to a specialist child and adolescent depression clinic, and were thus highly selected for the severity of their depressions. Subjects in the Angold et al. study were selected on the basis of their parent’s psychiatric status, rather than on the basis of their own symptomatology. The availability of data about the full range of depressive symptoms depended only upon their reporting that they had an episode of depressed mood or anhedonia at some time. Ryan and his colleagues also presented only combined analyses for boys and girls, and this may have obscured age trends which Angold et al. found to be confined to the girls. Though both groups used versions of the K-SADS for their psychiatric assessments, Ryan et al. and Mitchell et al. had the same interviewer interview both parents and children, and then reconcile disagreements in ratings with the interviewees, following which summary ratings were made. This procedure might also have obscured age effects that were limited to self-report data, since Angold et al. found no age effects in parent reports.

Despite these problems, there is consistency in the finding that sleep and appetite disturbances are more common in adolescent than childhood depressives. But we do not know whether these changes are specific to depression or reflect more general changes in sleep and appetite that are characteristic of adolescence itself. Further evidence of the need to consider developmental progressions in symptomatology is found in sleep studies of depressed children, which suggest that sleep disturbance only emerges in relation to depression in later adolescence (Puig-Antich, 1986) and from epidemiologic studies which show dramatic increases in rates of suicidal behavior in adolescence (Shaffer, 1982). It is also noteworthy that boys and girls show different patterns of change in suicidality, with boys having higher rates of completed suicide, while girls have much higher rates of non-fatal self-harm.

In summary, the current literature on patterns of depressive symptomatology indicates that there are changes in both patterning of depressive symptoms and rates of depression between childhood and adolescence, and that these pattern and rate changes are sexually dimorphic.

An overview of the physiology of puberty

Fig. 1 presents a visual overview of the morphological and hormonal changes of puberty (based in part on Lee, 1980, and references cited in Worthman, 1992).

Although the hypothalamo-gonadal-adrenal axes show a brief burst of activity in the first months after birth (reviewed in Skuse, 1984), circulating concentrations of gonadotrophins, and gonadal and adrenal steroids are very low in early to mid-childhood. Increases in adrenal androgen output (adrenarche) occur at around ages 6–8 years (Sizonenko and Paunier, 1975; Ducharme et al., 1976; DePeretti and Forest, 1976; Reiter et al., 1977; Parker et al., 1978; Lashansky et al., 1991). Adrenarche precedes the earliest changes of puberty on the hypothalamo-pituitary-gonadal axis by about 2 years and was initially thought to act as a trigger for its onset (Collu and Ducharme, 1975), but clinical and other studies have subsequently shown this to be untrue (Korth-Schutz et al., 1976; Wierman et al., 1986; Counts et al., 1987). The precise developmental role of adrenarche remains unclear, but it is still suspected to play a facilitative role in initiation of puberty.

Onset of puberty has long been thought to be characterized by the appearance and progressive
amplification of sleep-entrained pulsatile release of gonadotropins (Kulin et al., 1976; Judd et al., 1977; Beck and Wuttke, 1980). But recent advances in immunometric methods have led to the recognition that a circadian pattern of pulsatile gonadotropin release of low frequency and amplitude appears in late childhood (Dunkel et al., 1990; Wu et al., 1990), and that the transition to puberty is a gradual rather than acute event mediated through physiological mechanisms that are probably operative at ages 8–12 years, or 1–3 years prior to the onset of morphological puberty (Wennink et al., 1989; Wennink et al., 1990; Wu et al., 1990). Endocrinologic onset of puberty is now seen as involving increased gonadotropin pulse frequency as well as amplitude, and is marked by the appearance of frequent, closely sleep-entrained nighttime pulses of luteinizing hormone (LH). Current evidence indicates that luteinizing hormone releasing hormone (LHRH) pulse amplitude and frequency increase across the late prepubertal to early and mid stages of puberty (Hale et al., 1988; Landy et al., 1992), and show progressive diminution of diurnal variation in early to mid puberty. Pulse frequency decreases in late puberty (although amplitude continues to increase in males) as LHRH release becomes more sensitive to negative feedback control from gonadal steroids (Wennink et al., 1989; Dunger et al., 1991; Marshall et al., 1991). An important sex difference established over the course of puberty is that females develop pulsatile Gonadotrophin Releasing Hormone (GnRH) release along with fluctuating estradiol and progesterone (Marshall et al., 1991). Maturational pattern of this process extends from before menar-

![Fig. 1.](image-url)
These neuroendocrine changes are reflected in morphological signs of puberty such as growth and the development of secondary sex characteristics, such as those rated by Tanner’s pubertal stages (see Fig. 1). These morphological changes have consistently been shown to reflect, albeit grossly, underlying endocrine change (Burr et al., 1970; Sizonenko et al., 1970; Lee and Migeon, 1975; Sizonenko and Paunier, 1975; Lee et al., 1976; Apter, 1980). Indeed, both chronological age and pubertal stage correlate with endocrine parameters, but hormone levels explain on average less than half the variance in morphological pubertal development and growth in girls, but as much as 80% in boys (Nottelmann et al., 1987a). The reasons for this difference in hormone-morphology correlations are unknown. Thus morphological pubertal stage is an imprecise index of individual endocrine status, especially in females.

Implications of the physiology of puberty for psychopathological research

Consideration of the biology of puberty in both sexes suggests several points that need to be incorporated into a developmental account of the relationship between puberty and depression:

1. Some hormone change is cryptic; that is, adrenarche in both sexes and the earliest endocrine changes of puberty (especially in boys) are not reflected in visible morphologic change. The possible psychological effects of these early endocrine changes have been little studied, both because studies of adolescents generally do not commence until ages 9 or 10 or even later, and because much of the research has been focused on the visible morphological events. However, intensive research that examines both visible markers and endocrine status has fairly consistently demonstrated that it is the endocrine, rather than the visible pubertal changes, that best predict negative/depressive affect at puberty (Paikoff et al., 1991; Susman et al., 1991).

2. The neuroendocrine process that initiates puberty occurs in the age window over which rates of depression probably begin to rise in girls (and perhaps tall in boys), that is age 9–11. This underscores the need to study endocrine change in late childhood and to use earliest elevation of gonadotropins and gonadal steroids along with morphological progression into puberty as markers of developmental maturation.

3. The pattern of relationship between endocrine and morphologic change is different in males and females: most growth and sex character development occurs in girls in the first half of puberty and before menarche, whereas extensive endocrine change occurs in boys before the external signs of androgenization appear (see Fig. 1). Thus, rapid physical transformations co-occur with the period of early, most rapid endocrine change in girls, but are delayed and temporally removed in boys. Thus it is often stated that puberty occurs about two years earlier in girls than in boys in Western countries, but while this is true of a marker such as peak height velocity, it is not true of the relative timing of menarche in girls and first emission in boys, or of the onset of sleep-entrained pulsatile gonadotrophin secretion, which occurs only a little later in boys than in girls (see Fig. 1).

4. ‘Pubertal status’ is not adequately described by a single parameter relating to degree of progression on a single developmental path. Even Tanner’s well-known stages of morphological puberty require separate ratings on a number of dimensions. Brooks-Gunn and Warren (1985) pointed to five parameters of pubertal change that could be relevant to psychopathological research:

(a) Maturational status: Where in development is each individual, and how does being at this point (as opposed to other points) impact on psychopathology?

(b) Maturational timing: Where in relation to others is each individual, and what impact does this relative status have on psychopathology?

(c) Maturational rate: How rapidly are the changes of puberty proceeding? The time taken to progress from Tanner Stage 1 to Stage 5 may be anything from a few months to several years.

(d) Maturational synchrony: To what degree are
the hormonal, physical, psychological and social processes of puberty synchronized in an individual?

(e) Differential salience of maturational events: From the point of view of an adolescent's social and psychological understanding, not all events of puberty may be equally salient. The development of breasts or menarche would seem to be highly personally salient, but the same cannot be said of the bone changes that are proceeding concomitantly with more obvious effects of puberty. Concentration on single salient events is not sufficient. The substantial literature on the impact of menarche has predictably led to no very satisfactory conclusions (Greif and Ulman, 1982; Moffitt et al., 1992) since to divorce one aspect of a complex process from its developmental matrix is often a recipe for confusion. Two further parameters of puberty are also worthy of consideration, though the first can be seen as a qualitative component of the differential salience of maturational events.

(f) The meaning of maturational events at the personal level. The onset of puberty seems likely to mean something very different to the shy, thin 12-year old who experiences greasy, spotty skin as a major manifestation of rising testosterone levels, and the outgoing 12-year old athlete who puts on muscle instead. It is also reasonable to suppose that such manifestations of hormonal activity will have rather different effects on their relationships with girls. Simmons (1992) found that pretty girls were more likely to regard the change in body shape that accompanies puberty negatively, and suggested that this was because puberty for them meant the loss of a valued asset, while for less attractive girls it offered new hope for the future. Given that negative self-evaluation is part of the symptomatology of depression it would be worthwhile to address the personal meaning of the events of puberty more directly in future research.

(g) Cultural and social effects on puberty. Puberty is often treated as though it were independent of cultural or psychological factors, but strong evidence suggests otherwise. Social arrangements and practices largely determine environmental quality (nutrition, family size and spacing, child care) which, in turn, has been repeatedly found to affect rate of growth and timing of puberty (Eveleth and Tanner, 1991; Bielicki, 1986). The secular trends to reduced age at menarche and increased height for age in childhood that have consistently paralleled improved health care, industrialization and regularization of diet around the world vividly illustrate the influence of social arrangements on maturation patterns. Environmental effects operate, moreover, on the intrafamilial level: for instance, sibling height for age correlates inversely with sib order, even when the effect of socioeconomic status is controlled (Mascie-Taylor, 1991). Saugstad (1989a; 1989b) has employed Scandinavian and other European data to suggest that trends to earlier maturation have been associated with increased rates of manic-depressive disorder, and decreased rates of schizophrenia.

Similarly, the association between puberty and depression may not be one-way. Psychopathology and stress can alter the pace of growth and maturation. Psychogenic growth retardation is a dramatic and severe instance (Pollitt and Leiber, 1980, but see also Skuse, 1984); anorexia nervosa presents a less uncommon example where the onset of fat gain appears to precipitate dieting, which in turn leads to developmental retardation with switching off of ovarian function (Condit, 1990). Finally, childhood stress (specifically, family conflict and father absence) has been suggested to influence both timing of menarche and attitudes toward interpersonal relationships (Belsky et al., 1991), though the empirical support for this notion is mixed (Moffitt et al., 1992). One might also consider whether depression itself or factors involved in risk for depression also influence the timing and progression of puberty.

Let us now turn to the current evidence linking pubertal change with depression.

Depression and the parameters of puberty

Status effects of morphological pubertal stage

Pubertal staging represents a convenient measure of maturational status which has been incor-
porated in numerous studies of puberty and depression. In the Isle of Wight study (Rutter et al., 1970), a rough observational measure of pubertal status predicted depressive feelings more strongly than did age. On the other hand, the large clinical study of Angold and Rutter (1992) found that controlling for age eliminated any significant effect of pubertal status on depressive symptomatology. Rutter et al. (1989) have also reported results from a second clinical study that showed no effect of morphological pubertal stage when age was controlled for in hierarchical regression models, but significant effects of age when pubertal stage was controlled. Several studies using status questionnaire assessments of psychopathology have also failed to find effects of morphological pubertal stage (Susman et al., 1987a; Susman et al., 1987b; Brooks-Gunn and Warren, 1989a; Paikoff et al., 1991; Olweus et al., 1988). Overall, therefore, there is little evidence to support the notion that morphological pubertal stage per se is a significant risk factor for depression.

Relative timing of morphological puberty

A substantial literature based upon observation or self-report of pubertal stage, but without direct hormonal measures, has addressed the effects of the relative timing of puberty. In summary, early puberty has been associated with a positive psycho-social impact in boys, and a negative impact in girls (reviewed in Stattin and Magnusson, 1990). But none of these studies used measures of psychopathology suited to diagnosing depression. Perhaps most pertinently, Stattin and Magnusson (1990) found that early developing Swedish girls reported more psychosomatic and depressive symptomatology, particularly more suicidal thoughts, than did later maturing girls. Both early and late maturers (but especially the former) had more documented psychiatric service contacts by early adulthood than those whose puberty was normative. These analyses emphasized that effects of puberty timing were mediated through the impact of early maturity on girls' social lives. On the other hand, Paikoff, Brooks Gunn and Warren (1991) found no effects of the age at which increased estradiol secretion occurred in their 1-year follow-up study using the CES-D or in their original cross-sectional data (Brooks-Gunn and Warren, 1989b). They did, however, find an effect of the degree of hormonal level change over time on depressive symptoms.

A provocative time effect has been reported by Petersen, Sargiani and Kennedy (1991), who found that in both boys and girls, peak growth velocity occurring prior to, or close to, a change in school was associated with the occurrence of depressive symptoms in both boys and girls. However, the relatively early occurrence in puberty of this change in girls (usually during Tanner Stages I-III compared with occurrence in Tanner Stages IV and V in boys) meant that this combination of circumstances was more common in girls. Such findings further reinforce the idea that the biological changes of puberty need to be examined in the context of normative and non-normative changes in other aspects of the developing adolescent's life.

Hormonal status, timing, and rate of change effects on depression

Associations of depression with levels of gonadal hormones and gonadotropins have been reported. Abnormalities in gonadotropin secretion and of gonadotropin releasing hormone have been found in depressed adult patients (see, e.g., Tolis and Stefanis, 1983) while follicle stimulating hormone (FSH) levels have been found to correlate positively with negative affect in normal men (Houser, 1979). Rapidly falling estrogen levels have been implicated in menstrual cycle-associated mood changes (e.g., Bardwick, 1976) which have, in turn, been linked with increased susceptibility to major depression (reviewed in (Warner et al., 1991). Increases in estradiol have been found to improve depressive symptoms in hypoestrogenic women (Montgomery et al., 1987). However, findings from this considerable literature are rather inconsistent and difficult to interpret (see Bancroft, 1991, for an excellent critical review).

The NIMH study of puberty and psychopathology (Susman et al., 1987a; Susman et al., 1987b; Nottelmann et al., 1987a; Nottelmann et al., 1987b) described a negative association of testosterone:estradiol ratio, sex hormone binding globulin, and androstenedione concentration with negative emotional tone, but only in boys. These
workers also report an association of early maturation (measured by estradiol and testosterone:estradiol ratio) with less negative emotional tone in boys, but more negative emotional tone in girls. Adrenal androgen levels correlated with negative emotional tone in boys, but not girls, while the opposite was the case for FSH (Susman et al., 1985). Overall, hormone concentrations were more strongly associated with affective behavior in boys than in girls. In a recent summary (Nottelmann et al., 1990), the authors comment "not only that it is useful to examine more than one group of hormones in a study of hormone-behavior relations but that it is important to examine such relations in the context of other developmental markers such as chronological age and pubertal stage." However, these authors also recognize that interpretation of their findings is compromised by the use of many statistical comparisons with a small sample. Likewise, Brooks-Gunn and Warren (1989a) found that negative affect increased in 10–14-year-old girls during rapid estrogen rise (early puberty), but that social factors and their interaction with estrogen change together explained more of the variance in negative affect scores than did hormonal status alone. This work has now been extended to include a 1-year follow-up of 72 girls from the original sample (Paikoff et al., 1991). A significant linear effect of estradiol level at time 1 on CES-D scores 1 year later was found. However, there was no such effect on time 2 scores from the Depressed-Withdrawal scale of the Youth Behavior profile or on mothers' reports of their daughters' depressive affect.

Puig-Antich (1987) reported growth hormone (GH) hypersecretion in response to insulin-induced hypoglycemia in prepubertal, but not adolescent girls, and suggested that rising estrogen levels had decoupled the GH response to ITT from the neuroregulatory mechanisms of depression.

These studies all point to an effect of the biological changes of puberty on depressive symptomatology. Since the pattern of pubertal maturation differs hormonally and physically in boys and girls, these biological factors offer a potential basis for explanation of sex-differentiated trajectories in depression rates. But the degree to which these trajectories relate to hormone changes per se, the associated visible changes of puberty, or other age-related psychological or social changes (Brown et al., 1986; Weissman et al., 1987; Bird et al., 1988; Orvaschel et al., 1988; Goodyer and Altham, 1991) remains unclear. A theme that has begun to emerge from several of these studies is the need to consider the physiological changes of puberty within the social context of the adolescent.

While behavioral-affective effects of pubertal endocrine change have received some study, possible effects of prepubertal endocrine change, or adrenarche, have not. Extensive epidemiological data on timing of adrenarche are not available; nearly all reports merely offer means and variance of circulating andrenal androgens by age, frequently by age groups. Unlike puberty, adrenarche is not characterized by hormone elevations from minuscule concentrations; rather, there is an accelerated rate of increase in mid-childhood. Thus investigators have not established clear criteria for adrenarche as a developmental stage. Nevertheless, it does appear that adrenarche (reflected in dehydroepiandrosterone-sulphate, androstenedione, and dehydroepiandrosterone levels) is discernable on average between ages 6 and 8, and is well established by ages 8 to 10. Although available evidence (DePeretti and Forest, 1976; Reiter et al., 1977; Parker et al., 1978) suggests that timing of adrenarche and levels of adrenal androgen output show considerable individual variation, that variation has not been well documented (in contrast to intense interest in variable timing of puberty), and its relationship to psychosocial development or to behavior remains unexamined. Researchers in the field of depression and adolescence have emphasized the gap in our knowledge of psycho-behavioral effects of adrenarche and prepuberty, and noted the need for earlier measures (at least at ages 7–9) to detect developmental continuities and discontinuities (Brooks-Gunn and Warren, 1992; Eccles and Buchanan, 1992).

Puberty and peri-menstrual mood disturbance

In contrast to extensive research on adult women (see Endicott, this volume), little atten-
tion has been given to the issue of perimenstrual mood disturbance in adolescence. Epidemiologic data are scant, and information on the etiology of PMS is even more limited. In a study of older adolescents (mean age 17.6 years) attending an adolescent health service (primarily for sexual or gynecologic concerns), a significant percentage reported premenstrual changes considered to be severe (59%) or extreme (43%) (Fisher et al., 1989). ‘Major’ or ‘minor’ depressive changes were retrospectively reported by almost two thirds of respondents, impaired social function by almost one half and impulsive behavior by over one third. Nada Raja et al. (1992) used an arbitrary cutoff of 1.5SD above the mean on their retrospective Dysmenorrhoea Questionnaire, which included 16 psychological items, either before or during menstruation, to define PMS in 15-year-olds. They found that having premenstrual syndrome (PMS) by this definition was associated with concurrently higher anxiety and inattention scores from the Diagnostic Interview Schedule for Children (DISC) (Shaffer et al., 1989), but not with higher depression scores. However, these analyses did not distinguish between those with psychological symptoms and those with physical symptoms of PMS, and contained many fewer items than the better-known adult PMS questionnaires. Thus, further work is necessary to settle the question of whether there is an association between PMS and depression in early adolescence.

It is surprising that the adolescent literatures on pubertal effects on depression and the adult literature on perimenstrual mood disorders have not led to the examination of the role of perimenstrual mood disturbance in relation to the increase in depression in adolescent girls. While it seems unlikely that the diagnostic epidemiological findings of increased rates of major depression in adolescent girls are entirely the result of mis-diagnosis of menstrual-related affective disturbances, the potential contribution of such disturbances to changes in affective symptoms reports with age can hardly be ignored. Given the uncertainty associated with the findings from retrospective studies discussed above, prospective studies beginning prior to menarche offer an opportunity for substantial progress in understanding the relationships between depression and perimenstrual affective disorders. In particular, such studies would allow us to determine the degree to which perimenstrual affective disturbances reflect exacerbations of pre-existing depressive symptomatology, de novo phenomena that are precipitated by the onset of menstruation, and/or precipitants or predictors of major depression.

Puberty and behavior problems – the need to consider comorbidity

Space does not permit a detailed review of the associations between hormonal and morphological puberty and behavioral problems (see Buchanan et al. (1992) for a very substantial review), but it is important to recall that the psychopathological changes of adolescence are far from being confined to the affective domain (Rutter, 1990). The high rate of comorbidity between depression and behavioral disorders (see Costello and Angold, 1993; Caron and Rutter, 1991) means that some apparent hormonal effects on depression may, in fact, be a byproduct of effects on non-depressive disorders that are themselves correlated with depression.

The evidence in this area, though limited, appears sufficient to suggest a need to incorporate measures of behavioral symptomatology and disorders in studies of the relationship between depression and maturation at adolescence. Such an approach is necessary for identification of effects specific to the affective domain. An illustration of the potential importance of considering comorbidity is offered by Angold and Rutter’s finding (1992) that the substantial age effects seen with affective disorders in a large clinical population did not apply to mixed disorders of conduct and emotions. The relative timing of maturational effects may also differentially affect behavioral and emotional problems (Buchanan et al., 1992). Longitudinal studies with systematic measurement of a wide range of psychopathology offer the best means of shedding further light on these problems.

Conclusions

Overall, evidence linking the changing rates of depression in adolescence with the biological
changes of puberty is inconclusive, but studies that have addressed this question are surprisingly few in number. Several weaknesses in the current literature further contribute to uncertainty in this area:

(1) None of the child and adolescent psychiatric epidemiologic studies have employed adequate measures of pubertal status (and most have not engaged the issue at all).

(2) None of the epidemiologic studies has addressed the question of the degree to which the apparent rise in depression in adolescent girls might be related to perimenstrual mood disorders.

(3) The relevant endocrine studies have been compromised by small sample sizes and limited scale measures of psychopathology. None has examined rates of depressive diagnoses or detailed ratings of psychosocial impairment secondary to depressive symptomatology.

(4) The endocrine studies have not employed epidemiologically adequate sampling strategies (Paikoff et al., 1991). No large-scale population studies of the hormonal changes of puberty in Western adolescents are available in the English language (or elsewhere, to our knowledge). Small sample size, assay variation across laboratories, and a focus on physiologic process (intra-population patterns) rather than comparative studies across populations has led to a wealth of excellent clinical studies (e.g., Winter and Faiman, 1972; Winter and Faiman, 1973; Lee and Migeon, 1975; Lee et al., 1976; Apter, 1980; Nottelmann et al., 1987a), but a dearth of normative value ranges based on large sample sizes. In particular, the literature on adrenarche is severely limited, and there is growing awareness of the need to begin the examination of the relationship between puberty and psychiatric disorders much earlier in life than has been done up until now.

(5) Many studies of both adults and children relating psychiatric parameters to sex hormones have measured single hormones, with results that have been consistently unhelpful (Bancroft, 1991). On the other hand, when multiple hormones have been measured, the use of multiple statistical tests with relatively small samples has led to interpretative problems.

(6) Although the multidimensional biochemical and physical changes of puberty extend over several years (commencing with adrenarche), no study has covered an age-range that spans this period, and few have included any longitudinal component. Only two studies have addressed the critical issue of the impact of change in pubertal status as a possible precipitant of depression.

(7) Too little attention has been paid to the theoretical complexity of the idea of an association between puberty and depression. Analyses are needed that simultaneously consider the dimensions of (a) pubertal status, (b) the relative timing of puberty, (c) the rate of change of pubertal status, (d) the synchrony of pubertal change, (e) the salience of the events of puberty, (f) the personal meaning of the events of puberty, (g) the cultural meaning of the events of puberty and (h) whether each of these dimensions is best understood as a vulnerability or precipitating factor.

(8) Despite reports that depression is often associated with disruptive behavior disorders and that testosterone is implicated in the genesis of adolescent aggressive behavior, particularly in males, only one study considers co-morbidity as a possible confounder of the effects of pubertal status on depression.

(9) No study of a representative population sample has employed methods adequate to the task of simultaneously identifying relationships between hormonal status, morphological status, psychiatric status (at the levels of symptoms, diagnoses and psychosocial impairment), and social factors such as family difficulties or psychosocial impairment, longitudinally.

(10) Most studies, both of the effects of age and gender on depression rates and of the relationships between puberty and depression, have considered only diagnoses or scale scores as measures of depression. However, the study of rates of individual symptoms is also indicated by evidence that age and gender do not affect all symptoms of depression equally. For instance, Nolen-Hoeksema, Girgus and Seligman (1991) found that in 3rd-graders followed for 18 months, boys had consistently higher levels of anhedonia and behavioral disturbance, as measured by the CDI, but that boys and girls scored equally on self-deprecation, physiological symptoms and dysphoric mood items.
A clear implication of this review is that the methods of intensive laboratory studies of relatively small groups need to be applied to large representative samples, observed at multiple points in time from prepuberty to early adulthood, if we are to understand the role of puberty in the development of depression. We recognize the difficulties and complexities involved in adopting such an approach, but cannot avoid the fact that development is not a simple process, and that all the evidence points towards multiple determination in depression. In our present state of knowledge, it appears that large epidemiological studies are needed if further substantial progress is to be made. On the other hand, we have, in the increase in female depression in adolescence, a well documented effect of large size that is a good candidate for such investigation, and technologies available for the measurement of pubertal hormones in general population studies. In sum, the relationship between puberty and sex differences in rates of depression is ripe for further investigation by developmental epidemiological studies.

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