Review

To what extent do oral contraceptives influence mood and affect?

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Abstract

Background: Studies examining the effects of oral contraceptives (OCs) on mood, affect, and affect variability are reviewed. Methods: MEDLINE and PsycLIT data bases were examined to identify studies that compared OC users with nonusers using daily ratings of mood, affect, or affect variability. Results: Compared to non-users, OC users experience less variability in affect across the entire menstrual cycle, and less negative affect during menstruation (i.e. withdrawal bleeding). In women with OC-related negative mood and affect change, potential mediators of the relation between OCs and mood or affect were identified: a history of depression, psychiatric symptoms, dysmenorrhea, and premenstrual mood symptoms prior to OC use; a history of pregnancy-related mood symptoms; a family history of OC-related mood complaints; being in the postpartum period; and age. Furthermore, a lower ratio of progesterone to estrogen is associated with more negative mood change in women with a history of premenstrual emotional symptoms, higher progesterone to estrogen ratios are associated with increased negative mood effects in women without such a history, and monophasic OCs have a greater stabilizing effect on mood than triphasic OCs. Limitations: The ‘survivor effect’, psychological factors, and indirect pharmacological effects (e.g. weight gain) have not yet been systematically investigated. Furthermore, most studies have examined only negative mood or affect, as opposed to both positive and negative affect and affect variability; and few affect studies have assessed potential mediators of OC-related affect change. Conclusions: While the only consistent OC-related mood effects experienced by most women are beneficial, a subgroup of women do experience negative mood change. Future research must focus on expounding the individual difference and OC-related risk factors for negative mood change. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

Mood change remains one of the controversial side effects of oral contraceptive (OC) use despite a great deal of research. Change in mood, specifically depression, is one of the most common reasons given for discontinuing OC use (Goldzieher, 1994). How-
ever, guidelines for the management of OC-related mood change have not been based on comprehensive reviews of prospective clinical studies (e.g. Dickey, 1998). In order to provide a comprehensive review of the OC literature, this paper will: (a) discuss the biochemical mechanisms for OC-mediated mood change; (b) clarify the distinctions between mood and affect, and categorical versus dimensional measurement approaches; (c) review the research on the relationship between OCs and affect; (d) review the research on individual difference variables and OC-related variables that predispose women to OC-related affect/mood change; (e) discuss limitations of previous research; and (f) suggest directions for future research in the area.

2. Biochemical theories: hormones and mood

Although no clear consensus exists as to how the estrogen and progesterone in OCs could affect mood, a number of mechanisms have been proposed (Sheehan and Sheehan, 1976; Moller, 1981; Slap, 1981; Roy-Byrne et al., 1984; Deijen et al., 1992; Patten and Love, 1993; Special Advisory Committee on Reproductive Physiology, 1994; Tuiten et al., 1995; Sherwin, 1996).

The most plausible explanations for hormone-mediated negative mood change include: (a) an estrogen-induced pyridoxine (one component of vitamin B₆) deficiency and subsequent decrease in serotonin and GABA levels due to the low affinity of the decarboxylases for pyridoxal phosphate (e.g. Slap, 1981; Patten and Love, 1993; McCarty, 2000), (b) a progesterone- and estrogen-mediated augmentation of GABA-induced inhibition and suppression of glutamate excitation (e.g. Ghazal et al., 1976; Smith et al., 1987), and (c) a progesterone-mediated increase in monoamine oxidase (MAO) activity, resulting in lower serotonin concentrations (e.g. Sheehan and Sheehan, 1976; Sherwin, 1996). Since estrogen induces brain progesterone receptors, it is also possible that estrogen potentiates any progestogenic effects on mood (Fink et al., 1998).

Although biochemical mechanisms for any positive mood effects of OCs are less frequently discussed in the literature, the most plausible mechanism involves an increase in serotonin levels due to an estrogen-mediated inhibition of the MAO pathway (Chakravorty and Halbreich, 1997). In fact, increases in estrogen are associated with site-specific increases in: (a) the density of 5-hydroxytryptamine ₂A (5-HT₃A) receptors, (b) the expression of genes for the 5-HT₃A receptor, and (c) serotonin transporter mRNA (Fink and Sumner, 1996; Fink et al., 1998).

In terms of an OC-related effect on affect variability, Felthous and Robinson (1981) suggest that monophasic OCs may stabilize affect across the cycle through stabilization of cycle fluctuations in estrogen and progesterone, resulting in a stabilization of the functional levels of the relevant central neurotransmitters.

3. Mood versus affect

Mood and affect are closely related terms that are often used interchangeably in the literature. There are, however, important and useful distinctions between the two concepts. The American Psychiatric Association (2000) compares mood and affect to climate and weather, respectively. Mood is referred to as “a more pervasive and sustained emotional ‘climate’” while affect involves “more fluctuating changes in emotional ‘weather’” (p. 819). Early research on the relationship between mood and OC use took a categorical approach by focusing on the presence or absence of diagnosable mood disorders in women who use OCs. Most studies looked at the incidence of clinical depression in OC users (e.g. Herzberg et al., 1970; Kutner and Brown, 1972a; Vessey et al., 1985). Another approach involves viewing mood as a dimensional continuum and measuring the positive or negative mood change occurring during OC use. The dimensional approach allows one to look at sub-clinical change and thus investigate changes in all women as opposed to only those who develop a mood disorder. It also allows

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1Guidelines have been based primarily on laboratory measurement of estrogenic, progestational, and androgenic activity of specific OC formulations, and hypothetical relationships between relative hormonal activity and specific mood symptoms.
for the measurement of change in both positive affect and negative affect (Watson and Tellegen, 1985).

Positive affect reflects the extent to which a person feels a zest for life. Someone with high positive affect is characterized as attentive, interested, alert, and enthusiastic. Someone with low positive affect feels sleepy and tired. Negative affect reflects the extent to which a person conveys feeling distressed or unpleasantly aroused. A person with high negative affect feels downhearted, hostile, angry, fearful, and guilty, while someone with low negative affect is characterized as calm and content. The rationale for measuring negative and positive affect separately comes from studies, summarized by Watson and Tellegen (1985), which have consistently found that positive and negative affect are dominant and relatively independent dimensions (e.g. Diener and Emmons, 1985; Kercher, 1992).

Thus, a categorical approach to investigating mood change associated with OC use is concerned with the development of a diagnosable mood disorder while the dimensional approach looks at short-term changes in mood or levels of negative and/or positive affect.

4. Early research: oral contraceptives and mood (categorical approach)

The early research7 on mood change associated with OC use has produced inconsistent findings. Most studies employed designs that assessed mood in never-users, past-users, and present users of OCs, one to three times over the course of several months. The early studies usually either compared rates of depressive disorders between the two or three groups (e.g. Royal College of General Practitioners, 1974) or compared scores on mood rating scales designed to measure general or average mood (e.g. Herzberg et al., 1970). Some researchers found increased rates of depression in OC users (e.g. Nilsson and Almgren, 1968; Herzberg et al., 1970; Cullberg, 1972), others found a decrease in depression rates (e.g. Herzberg et al., 1971; Deijen et al., 1992), and some studies did not find any relationship between OC use and incidence of depression (e.g. Fleming and Seager, 1978; Vessey et al., 1985). While many reviews of this early research are incomplete, Slap (1981), Cullberg (1972), and Long and Kathol (1993) include most of the better studies.

5. Recent research: oral contraceptives and affect (dimensional approach)

More recent studies have focused on differences in affect by having subjects fill out daily self-rating scales for 30–90 days (e.g. Walker and Bancroft, 1990; Almagor and Ben-Porath, 1991). Daily rating scales can be used to examine cyclical changes in affect across the menstrual cycle and general trends or differences in mood between the OC users and non-users. This methodology also permits mood variability to be assessed, and allows researchers to identify changes that might occur at specific phases of the menstrual cycle. Daily mood ratings, or more accurately, daily ratings of affect, are a more sensitive indicator of differences between users and non-users of oral contraceptives.

A review of the literature revealed 17 studies comparing daily ratings of affect in both OC users and non-users8. Given the limitations of retrospective designs, four studies were not included in the present review (Moos, 1968; Rouse, 1978; Warner and Bancroft, 1988; Bancroft and Rennie, 1993). Examination of the results of the 13 controlled prospective daily-rating studies revealed that all but one study (Marriott and Faragher, 1986) found group differences in affect between OC users and non-users. However, the direction of the differences and the menstrual cycle phases in which the differences occurred were not consistent across studies.

Since most researchers divided the menstrual cycle

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7It is important to keep in mind that a major reduction of the estrogen dosage in oral contraceptives occurred in 1985.

8Studies were excluded if there were no published statistical analyses or raw data to examine differences in affect between OC users and non-users (e.g. Gallant et al., 1992), or if a control group of non-OC users was not included in the study (e.g. Forrest, 1979; Alexander and Sherwin, 1993; Tuiten et al., 1995). [Bancroft and Sartorius (1990) review a number of the studies covered in the present review and include an excellent broad review of methodological considerations and the effects of OCs on well-being and sexuality.]
into different phases, the four most frequently used phases were used for this review: all days of menstrual flow (menstrual phase), the 7 days after menstruation (postmenstrual phase), the remaining days leading up to the 7 days before menstruation (intermenstrual phase), and the 7 days before menstruation (premenstrual phase). (Although, technically speaking, women taking OCs experience withdrawal bleeding as opposed to menstruation, the bleeding phase of the cycle will be referred to as the menstrual phase for all women, as is common in this literature.) Three types of findings are summarized below: group differences in affect, group differences in affect variability, and group differences during each of the four phases of the menstrual cycle. While most studies examined negative affect, a few studies also examined positive affect.

The majority of the studies found no significant group differences in negative affect across the entire menstrual cycle (Paige, 1971; Wilcoxon et al., 1976; Marriott and Faragher, 1986; Almagor and Ben-Porath, 1991). While one study found that OC users feel less negative affect across the cycle (Boyle and Grant, 1992), one study found that monophasic OC users experienced higher negative affect throughout the cycle (Walker and Bancroft, 1990). In terms of positive affect, Almagor and Ben-Porath (1991) found that OC users experienced higher positive affect. Two other studies, however, did not find group differences in positive affect (Silbergeld et al., 1971; Boyle and Grant, 1992).

The ingestion of the hormones in OCs does provide a stabilizing effect on mood. Four studies found that OC users showed less day-to-day variability in their affect ratings than non-users (Paige, 1971; Sutker et al., 1983; Walker and Bancroft, 1990; Graham and Sherwin, 1993). Only one study (McFarlane et al., 1988) did not find any significant differences in affect variability between the two groups. It is noteworthy that researchers have not examined group differences in positive affect variability across the menstrual cycle, or group differences in circadian affect variability.

When group differences in negative affect within specific menstrual cycle phases were examined (Paige, 1971; Morris and Udry, 1972; Wilcoxon et al., 1976; Sutker et al., 1983; Marriott and Faragher, 1986; Alexander et al., 1990; Walker and Bancroft, 1990; Almagor and Ben-Porath, 1991; Boyle and Grant, 1992; Graham and Sherwin, 1993), only the findings from the menstrual phase were relatively consistent. While three studies did not find any group differences in negative affect during the menstrual phase (Alexander et al., 1990; Almagor and Ben-Porath, 1991; Graham and Sherwin, 1993) and one study found higher negative affect for monophasic, but not triphasic, users (Walker and Bancroft, 1990), four studies suggest that OC users experience less negative affect than non-users during the menstrual phase (Paige, 1971; Wilcoxon et al., 1976; Sutker et al., 1983; Boyle and Grant, 1992). Although three of these studies did not provide an interpretable statistical analysis of the comparison (Paige, 1971; Sutker et al., 1983; Boyle and Grant, 1992), graphs or data suggested consistent trends in the direction of OC users experiencing less negative affect than non-users during menstruation. This reduction in negative affect could, of course, be the consequence of an OC-mediated reduction in somatic symptoms (i.e. an indirect pharmacological effect). Three of these studies that examined somatic symptoms did, in fact, find lower levels of physical symptomatology in OC users than non-users during menstruation, but it was not possible to establish the extent to which this OC-mediated reduction in physical symptoms could account for the lower negative affect in OC users. This remains an interesting and viable explanation, however.

Although four studies (McFarlane et al., 1988; Walker and Bancroft, 1990; Almagor and Ben-Porath, 1991; Boyle and Grant, 1992) measured positive affect over the menstrual cycle, there is no consistent difference in positive affect between OC users and non-users during any of the menstrual cycle phases.

6. Risk factors or predisposing factors to mood/affect change

6.1. Individual difference variables

As reviewed above, the only common effects of OCs on affect for all women are better described as beneficial than adverse effects (i.e. less variability in negative affect across the cycle and less negative
affect during menstruation). However, the fact that
some women do experience OC-related increases in
negative affect/mood (Canadian Pharmaceutical As-
association, 2000) suggests that individual difference
variables predispose certain women to specific OC-
mediated changes in mood or affect. The majority of
research on such variables has focused on OC-
related changes in mood or depression. Only a few studies
have examined specific individual difference vari-
abless that may increase the likelihood of OC-me-
mediated changes in affect. Furthermore, very few of
the studies were conducted using the low-dose OCs
that are currently in use.

Previous studies suggest that the following vari-
abless increase a woman’s risk of becoming depressed
or exhibiting depressive symptoms when taking OCs:
(a) a history of depression (Nilsson et al., 1967;
Lewis and Hoghughi, 1969; Herzberg et al., 1971);
(b) a history of moderate to severe ‘premenstrual depression’ (Herzberg and Coppen, 1970) or severe
premenstrual weepiness prior to OC use (Herzberg et
al., 1971); (c) a history of dysmenorrhea prior to OC
use (Herzberg and Coppen, 1970); (d) a history of
depression during or after pregnancy (Nilsson et al.,
1967; Herzberg et al., 1971; Kutner and Brown,
1972b); (e) a family history of OC-related depressive
symptoms (Kendler et al., 1988); (f) a predisposition
to a vitamin B$_6$ deficiency while taking OCs (Adams
et al., 1974; Wynn et al., 1975), and (g) a high level
of psychological distress prior to OC use (Cullberg,
1972; Tuiten et al., 1995). While one study found
that a history of psychological distress was not
associated with an increase in symptoms of depres-
sion (Grounds et al., 1970), this study only examined
the first 2 months of OC use.

Two studies suggest that the following variables are
unrelated to the development of depression while
taking OCs: age; age at menarche; length of menstru-
al cycle; parental separation, divorce, or death; birth
weight; feeding problems or serious illness during
the first year of life (Herzberg et al., 1971); educa-
tion; religion; and family size (Murawski et al.,
1968).

Only four studies have investigated individual
difference variables that predispose women to OC-
related changes in affect. Bancroft and colleagues
(1987) found that women younger than 20 ex-
perienced more negative affect, or perhaps less
positive affect, during days 13–18 of OC use than
older women. This is in line with the finding that
women older than 30 experience less tension than
non-users during menstruation while taking OCs
(Rouse, 1978). Therefore, while women under age
20 are more likely to experience an increase in
negative affect, women over 30 experience a de-
crease in negative affect. Another study found that
women who are premenstrually ‘depressed’ at
baseline show greater improvement in behavioural
positive affect measures premenstrually than ‘non-
depressed’ women while taking a triphasic OC
(Graham and Sherwin, 1992). A final study ex-
amedined the following variables and found that they
could not account for the observed differences in
negative affect variability between monophasic OC
users and non-users: age at menarche, reaction to
menarche, mother’s attitude to menstruation, amount
of preparation for menstruation, degree of menstrual
discomfort during teens, and prior expectations about
the effects of OCs on mood (Paige, 1971).

6.2. Oral contraceptive-related variables

As well as the individual difference variables
noted above, there are a number of OC-related
variables that may affect women directly or interact
with other variables to influence mood or affect. For
example, OCs can differ in terms of constituents
(types of estrogen and progesterone), dosage, ratio of
progesterone to estrogen, and temporal pattern of
dosage (monophasic, biphasic, or triphasic). A num-
ber of these variables have been investigated in terms
of their effects on mood and a few in terms of their
effects on affect.

While there is a consensus that high doses of both
estrogen and progesterone in OCs are associated with
an increase in negative mood side effects (e.g. Deijen
et al., 1992), there is no consensus of findings
indicating whether higher doses of progesterone,
higher doses of estrogen, or specific ratios of these
hormones are likely to increase the risk of mood or
affect change for all women. Four studies suggest
that OCs with either higher dosages of progesterone
or higher ratios of progesterone to estrogen produce
more depression or negative mood effects (Peterson,
1969, cited in Cullberg, 1972; Grant and Pryse-
Davies, 1968; Lewis and Hoghughi, 1969; Akerlund
et al., 1993). Interestingly, in the study by Akerlund and colleagues, when the progesterone dosage was held constant, women taking the OC with the lower estrogen dosage reported more negative mood change. In contrast, a large-scale study indicated that rates of depression increase as estrogen dose increases (Kay, 1984) and two studies found that lower dosages of progesterone or lower ratios of progesterone to estrogen were associated with greater symptoms and severity of depression (Cullberg, 1972; Kutner and Brown, 1972a). Another study found that the dosage of progesterone was unrelated to rates of depression (Kutner and Brown, 1972b). The inconsistency in the findings suggests the possibility of a third variable that moderates the relationship between progesterone or estrogen dosage and subsequent mood or affect change.

Two excellent studies indicate that premenstrual mood symptoms moderate the relationship between type of hormone, dosage, and negative mood change (Bancroft et al., 1987; Cullberg, 1972). Women with a history of premenstrual irritability/emotionality prior to OC use had an increased risk of negative mood effects if they took an OC with lower progesterone levels or lower progesterone to estrogen ratios. Furthermore, women without a history of premenstrual irritability/emotionality had an increased risk of negative mood effects if they were taking an OC with higher progesterone levels or higher progesterone to estrogen ratios. The interaction between progesterone dosage and premenstrual irritability history on mood suggests that history of premenstrual emotional symptoms should be considered when selecting an OC.

The relative effects of monophasic, biphasic, and triphasic OCs on mood and affect have also been examined. Although two studies did not find any difference in rates of severity of depression between monophasic, triphasic, and non-users (Herzberg et al., 1970; Bancroft and Rennie, 1993), three studies suggest that monophasic OC use is associated with greater mood stability than triphasic OC use (Moos, 1968; Warner and Bancroft, 1988), biphasic OC use (Paige, 1971), and no use (Paige, 1971; Warner and Bancroft, 1988). Kutner and Brown (1972a) also found that monophasics are associated with less ‘premenstrual depression’ than biphasics.

While one study examining affect found that monophasic users experience more negative affect compared to triphasic users and non-users (Walker and Bancroft, 1990), the subjects were all experiencing premenstrual symptoms while taking OCs and had been taking OCs for a mean of 3.7 years. Thus, the research indicates that monophasic OCs stabilize mood, and as illustrated in the study by Bancroft and colleagues (1987), are much less likely than triphasic OCs to cause negative mood changes in women with high baseline premenstrual emotional symptoms.

An examination of research on OC discontinuance and duration of use indicates that the severity of premenstrual irritability symptoms increases over time after OC discontinuance (Kutner and Brown, 1972a), and that there are contradictory findings regarding whether duration of pill use is related to depression (Herzberg et al., 1970; Kutner and Brown, 1972a). Given that the ‘survivor effect’ (discussed below) may account for some of the inconsistency in studies on the relationship between affect and OCs, duration of use should be investigated further.

The review of OC-related variables that affect mood/affect suggests three conclusions. First, for women with a history of premenstrual emotional symptoms prior to OC use, OC formulations with higher progesterone to estrogen dosage ratios are associated with less negative mood changes, as are the use of monophasic versus triphasic OCs. Second, for women without a history of premenstrual irritability, formulations with lower ratios of progesterone to estrogen decrease the risk of negative mood change. Finally, adding to the earlier discussion about the stabilizing effects of OCs on mood, monophasic OCs have a greater stabilizing effect than triphasic OCs.

7. Problems with previous studies

The above review reveals that future research must: (a) control for the ‘survivor effect’ (discussed below) and duration of OC use, (b) independently measure both negative and positive affect, (c) expound mediating or moderating individual difference or OC-related variables for specific types of affect change, (d) assess group differences in both negative and positive affect variability, and (e) control for
three potentially important psychological or indirect pharmacological variables.

The ‘survivor effect’ (Kutner and Brown, 1972a) refers to the fact that women who experience problems while taking OCs stop taking them, which, by definition, leaves a group of women who are not experiencing adverse effects (mood or otherwise). Roughly 25% of women discontinue OC use within 1 year of use (Trussell and Kost, 1987) and depression is in fact one of the most common reasons given for discontinuation (Kay, 1984). Therefore, the incidence rates of negative mood change associated with being on OCs are likely underestimations in studies using groups of women taking OCs for many years, since any women who experience moderate to severe negative mood effects would likely have discontinued use.

Three factors can contribute to the survivor effect: (a) the selection criteria for the OC user and non-user groups, (b) the length of time which the OC users have been taking the OC pill, and (c) the study’s attrition rate. In order to minimize survivor effects, researchers should distinguish between first-time users and brand ‘switchers’ in the OC user group, and between never-users and previous-users in the non-user group. The inclusion of ‘switchers’ in the user group and of previous users in the non-user group introduces a bias, since it may have been negative mood effects which led to switching brands or discontinuing use (i.e. Deijen et al., 1992). With regards to duration of pill use, it is important to distinguish between ‘early’ and ‘late’ use of OCs (e.g. Bancroft and Sartorius, 1990). While an early-use group would still contain women who may discontinue OCs in the future due to negative effects, a late-use OC group would have already lost the women experiencing negative mood side effects. Finally, in prospective studies and controlled experiments comparing OC users and non-users, large attrition rates increase the size of the survivor effect. It seems logical that a woman just starting on the pill who drops out of an experiment would be more likely to do so as a result of negative than positive mood side effects. Losing this type of data makes the OC users groups appear to be experiencing less negative affect than they actually are. The ‘survivor group’ would include women who are taking OCs and potentially experiencing no mood effects, positive mood effects, or only mild negative effects on mood.

A second suggestion for future research is to use independent measures of change in positive affect, negative affect, positive affect variability, and negative affect variability. If women’s subjective complaints of OC-related increased depression or negative affect, or increased moodiness or lability, actually reflect decreased positive affect and increased positive affect variability, respectively, traditional measurement of negative affect and negative affect variability will not identify such differences. Given the independence of positive and negative affect, separate measures of these dimensions are required to detect any effects of OCs on affect or affect variability.

A third suggestion is to evaluate individual difference variables and OC-related variables associated with specific OC-related affect changes. While many of the studies reviewed above examined predisposing variables for OC-related depression, very few studies have focused on examining such risk factors for changes in positive and negative affect and affect variability. If OC-related affect change varies as a function of OC type, a failure to separately analyse users of monophasic, biphasic, and triphasic OC preparations may make it difficult to detect mood change if women taking different OC types are grouped together. Morris and Udry (1972) found that of the OC users who felt ‘differently’, one-half felt ‘better than usual’ and the other half felt ‘worse than usual’. This suggests that if some women experience increased negative affect and others experience decreased negative affect with OC use, a failure to separately examine these groups means that any negative affect changes may cancel each other out if the overall mean of OC users is compared with non-users. Obviously, a failure to separately examine groups of women experiencing different types of mood change can result in an obfuscation of actual mood change as well as an increased likelihood of overlooking potentially important predisposing individual difference and OC-related variables.

As reviewed above, women taking OCs experience less variability in negative affect than non-users. It may be that affect variability, rather than average affect, is primarily altered by OCs. This hypothesis suggests the importance of assessing
group differences in positive as well as negative affect variability. Furthermore, diurnal and ultradian variation in mood has long been observed in affective disorders and there are known diurnal and circadian rhythms in neuroendocrine activity (e.g. adrenocorticotropic hormone, cortisol, growth hormone, thyroid stimulating hormone; Goodwin and Jamison, 1990; Checkley, 1992; Thase and Howland, 1995). Unfortunately, studies comparing OC users and non-users have failed to examine within-day variability in affect.

A fifth suggestion is to control for three possible psychological and indirect pharmacological causes of mood change due to OC use (e.g. Cullberg, 1972). First, expectations of a positive or negative mood change side effect can lead to mood change (or the placebo effect; e.g. Cullberg et al., 1969). Second, what Cullberg (1972) refers to as the “symbolic effect of the ‘anti-baby pill’” may also lead to changes in mood (e.g. increased negative affect due to feelings of guilt over preventing the conception of a child, or mood improvements due to increased reassurance about pregnancy prevention). Third, mood changes may also occur secondary to somatic side effects (an indirect pharmacological effect) (e.g. increased negative affect following weight gain or increased positive affect following a desired breast size increase). Since these factors could hypothetically lead to an improvement or deterioration in mood, pre-test measures of each should be included when attempting to determine the cause of a mood change associated with OC use. However, it is important to realize that the correlation of any of the three factors with the predicted mood change does not rule out the possibility of a pharmacological effect.

8. Conclusions

A number of plausible biochemical explanations have been put forward to explain how the estrogen and progesterone in OCs could have effects on mood or affect. As the dimensional approach of studying affect is more sensitive than the categorical approach of examining rates of mood disorders, studies that compared daily ratings of affect in OC users and non-users were reviewed. Compared to non-users, women taking OCs experience less variability in affect across the menstrual cycle and less negative affect during the menstrual phase. Research also suggests that the following factors predispose certain women to OC-related negative changes in mood/affect: a history of depression, other symptoms of psychological distress (e.g. anxiety, stress, neuroticism), dysmenorrhea, and premenstrual mood symptoms prior to OC use; a history of pregnancy-related mood symptoms; a family history of OC-related mood complaints; being in the postpartum period; and age. A number of OC-related variables also mediate mood/affect change for certain individuals: types of estrogen and progesterone in the OC; dosage; ratio of progesterone to estrogen in the OC; temporal pattern of dosage; and duration of OC use. More specifically, women with premenstrual mood symptoms prior to OC use experience more negative mood symptoms when taking OC formulations with lower progesterone to estrogen dosage ratios or when taking triphasic (versus monophasic) OCs. Second, for women who do not complain of premenstrual irritability, formulations with higher ratios of progesterone to estrogen increase the risk of negative mood change. Finally, monophasic OCs have a greater stabilizing effect than triphasic OCs on mood.

In the OC literature it is commonly suggested that, due to the 1985 estrogen reduction in OCs, there is no need for concern about the possibility of OC-related negative affect change. However, four factors suggest that the above individual difference and OC-related variables cannot be discounted as predisposing factors or mediators for negative mood change. First, women continue to experience negative mood effects while taking OCs (Canadian Pharmaceutical Association, 2000). Second, some studies have indicated that OCs with lower estrogen dosages are associated with more negative mood complaints (e.g. Akerlund et al., 1993). Third, while the earlier studies included women taking higher dose OCs than are commonly taken today, most of the studies also included a substantial number of women taking OCs that have equivalent estrogen dosages to formulations prescribed today (e.g. Herzberg et al., 1971; Kutner and Brown, 1972a). Fourth, while only a few recent studies have examined individual difference and OC-related mediating factors in mood/affect change (e.g. Bancroft et
al., 1987; Warner and Bancroft, 1988; Akerlund et al., 1993), there are no studies that contradict the earlier findings.

Other individual difference variables deserving exploration include physiological measures such as baseline levels of endogenous hormones (e.g. estrogen, progesterone, cortisol), personal and family medical history indicators (e.g. thyroid disorders, breast cancer, and diabetes), and variables indicative of differential hormone sensitivity (e.g. body mass index, waist-to-hip ratio or body fat distribution, acne history, and menses duration).

Another important area of future research involves the examination of the interaction between OC type and the lipid, lipoprotein, and hormone parameters known both to be affected by OCs and to be associated with changes in mood or affect. For example, while the use of some OCs is associated with a decrease in total cholesterol, LDL cholesterol, and triglyceride levels (e.g. Wiegartz et al., 1998; Mostafavi et al., 1999; Stefanick, 1999), the use of other OC types is associated with increases in total cholesterol and triglyceride levels (e.g. Schiele et al., 1998; Wiegartz et al., 1998; Cheung et al., 1999; Mostafavi et al., 1999). These changes may play an etiological role in OC-related mood change as some studies have indicated an association between higher levels of depression and anxiety and low levels of total cholesterol, triglycerides, and LDL cholesterol (Olusi and Fido, 1996; Suarez, 1999). Other studies have found associations between high triglyceride and cholesterol levels and Generalized Anxiety Disorder (Kuczmieryk et al., 1996), and high triglyceride levels and depressive symptoms (Glueck et al., 1993). Some women may be more sensitive to OC-related changes in lipid parameters and/or any effects of lipid parameters on mood. With further research it may be possible for physicians to choose an OC least likely to cause mood change, based on a woman’s baseline lipid levels, the known effects of each OC type on lipid levels, family and personal physical/psychiatric history, as well as information about behavioural factors known to affect lipid levels (e.g. diet, exercise, and drug use). While the effects of OCs on lipid levels have been investigated and monitored in order to prevent cardiovascular disease, these same variables deserve further attention as possible mediators in OC-related affect change.

In addition, a number of methodological guidelines could improve future research. While these guidelines may seem obvious, they should be restated given the fact that, despite over 40 years of research, many questions remain unanswered about the relationship between OCs and mood or affect changes. Moreover, recent studies (e.g. Haugen et al., 1996; Sivin et al., 1998) investigating potential side-effects of subdermal contraceptive implants are limited by many of the same methodological problems as the early OC studies. First, subjects taking OCs should be defined as long-time users or first-time users, and non-users should be defined as previous-users or never-users. Any long-time user study may underestimate negative mood side effects due to the survivor effect. Second, all studies should use prospective, as opposed to retrospective, ratings of affect. Third, independent measures of positive and negative affect should be included as both types of mood change have been reported. Fourth, group differences in both positive and negative affect variability should be examined as OCs provide a stabilizing effect on mood. Fifth, the effects of OCs on the variability of circadian and ultradian rhythms as well as daily ratings of affect should be examined. Finally, psychological (e.g. expectations) and indirect pharmacological factors (e.g. somatic changes such as weight gain) that could affect mood should be assessed to determine what role, if any, they may play.

In response to the original question posed in the title of this article, the only OC-related effects on mood that are experienced by most women are positive: mood stability and decreased negative affect during menstruation. However, a subgroup of women also experience negative mood effects, and specific individual difference and OC-related variables increase one’s risk of experiencing these negative effects.

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