Mood disorders in oocyte donor candidates: brief report and implications for future research

Katherine E. Williams1,*, Pascale G. Stemmle2, Lynn M. Westphal3, and Natalie L. Rasgon1

1Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Road, Room 2358, Stanford, CA 94305-5723, USA
2PGSP-Stanford Psy.D. Consortium, Palo Alto, CA, USA
3Department of Obstetrics and Gynecology, Stanford University School of Medicine, Stanford, CA, USA

*Correspondence address. Fax: +650 724-3144; E-mail: elliew@stanford.edu

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BACKGROUND: IVF, using donor oocytes, has become increasingly common. The donation procedure carries psychiatric risks, including depression, anxiety and rarely, psychosis, and this risk increases when there is a past history of psychiatric illness. We report on the psychiatric status, at intake assessment, of a group of candidate oocyte donors.

METHODS: The authors reviewed clinical records of 63 women continuously presenting to a University medical center for psychiatric evaluation as part of the screening process for oocyte donation. A board certified psychiatrist administered a structured clinical interview to candidate donors, and self-report measures were obtained from 28 women.

RESULTS: There was a significant discrepancy between psychiatric history of depression and current mood status, as measured by both clinical interview and psychometric self-report data. Nearly one-quarter of candidate donors (22%) reported a history of major depressive disorder; however, all candidate donors denied current mood disturbance on clinical interview, and mean Beck depression inventory and profile of mood states scores were lower than expected compared with psychometric norms (P < 0.0005), epidemiological data and the recurrent nature of depressive disorders.

CONCLUSIONS: Candidate donors may minimize psychiatric symptoms. Given the potential for ovarian stimulation protocols to induce or exacerbate mood symptoms, and the moderate heritability of mood disorders, careful evaluation of candidate donor affective disorder history is recommended. This evaluation should focus on sensitivity to mood destabilization during times of hormonal change. Measures that examine whether a candidate donor may have a tendency to present herself in an overly favorable manner, and/or a tendency to minimize symptoms, are recommended.

Key words: oocyte donation / psychiatric / depression / screening / donor evaluation

Introduction

IVF using donor oocytes has become an increasingly common assisted reproduction procedure for the treatment of premature ovarian failure, heritable genetic problems, recurrent IVF failure and advanced maternal age. In the USA in 2005, 10 620 fresh donor cycles and 5541 frozen donor cycles were initiated (Centers for Disease Control, 2007). However, very few studies have investigated the demographic and psychiatric characteristics of candidate oocyte donors (Schover et al., 1991; Sauer and Paulson, 1992; Lessor et al., 1993; Greenfeld et al., 1995; Klock et al., 2003). Understanding the psychiatric characteristics of potential oocyte donors is important since the donation process itself is not without procedural and/or psychiatric risk. The procedural risks of oocyte donation include ovarian hyperstimulation syndrome, infection and ovarian torsion (Maxwell et al., 2008).

In addition, the medications involved in an ovarian stimulation protocol have been associated with psychiatric side effects (Choi et al., 2005). Several investigators have reported that GnRH agonists, such as leuprolide acetate, are associated with increased depressive and anxiety symptoms (Toren et al., 1996; Grigorova et al., 2006). Women taking hMG report a high frequency of psychiatric side effects, including irritability, mood lability and depressed mood (Choi et al., 2005). Since several epidemiological and experimental studies suggest that a subgroup of women may be especially vulnerable to the onset or recurrence of psychiatric symptoms at times of hormonal change (Habreich, 2010), the process of oocyte donation...
may carry particular risk for the exacerbation or relapse of a pre-existing psychiatric illness. The purpose of the current study is to report on the psychiatric clinical status, at intake assessment, of a group of donor candidates in a university-based oocyte donor program.

Material and Methods

Procedure

After receiving approval from the University’s Institutional Review Board, trained staff reviewed clinical records of candidate oocyte donors who were continuously evaluated by the author (K.E.W.) at the Department of Psychiatry at Stanford Medical Center between 1998 and 2003. The author, (K.E.W.) who is certified by the American Board of Psychiatry and Neurology and is a specialist in women’s mental health, conducted clinical intake assessments of each donor candidate. The Reproductive Endocrinology and Infertility team used the results of this intake in order to determine eligibility for oocyte donation. Each intake interview carefully followed guidelines established by the American Society of Reproductive Medicine (ASRM, 1998), and was conducted in a structured manner to enable data to be systematically extracted from the interviews. Because these intakes were conducted between 1998 and 2003, the interview and screening process adhered to ASRM guidelines of that time, not the newest guidelines available (ASRM, 2008).

The aim of this brief report is to describe the psychiatric history and demographic characteristics of a sample of women screened to become oocyte donors, compare these characteristics to existing literature on mental health in oocyte donors, and provide recommendations for future research in this field.

Sample

Sixty-three women of reproductive age were continuously evaluated for potential oocyte donation and demographic characteristics were recorded. Donor candidates ranged in age from 20 to 37 years. Donor candidates were classified as identified if they had volunteered to donate oocytes to someone they had a prior relationship with, such as family members or friends. Donor candidates were classified as anonymous if they had no prior relationship with the recipient. The group of anonymous donors answered advertisements or were recruited individually or through agencies for oocyte donation. Approximately one-third (36.5%) of candidates were identified donors, and the majority of these were family members of the recipient (n = 17), while a handful (n = 6) were close friends of the recipient.

Instruments

Self-report data were available for analysis for 28 candidate donors. There were no statistically significant differences in demographic or clinical variables, including psychiatric history, between groups for those in whom self-report data were available and those for whom these data were not available.

Profile of mood states

The profile of mood states (POMS) is a 65-item self-report mood symptom checklist (McNair et al., 1971). The 65 items form 6 subscales. Five of the subscales reflect negative mood states, including tension–anxiety (tapping both somatic and subjective feelings of anxiety), depression–dejection (tapping feelings of worthlessness, hopelessness, isolation, guilt and sadness), anger–hostility (tapping overt feelings of anger toward others and irritability), fatigue–inertia (tapping weariness or low energy level), and confusion–bewilderment (tapping cognitive efficiency). One subscale, vigor-activity, reflects positive mood, including feelings of friendliness and ebullience. For each item, respondents rate the presence of different types of feelings over the past week from 0 (not at all) to 4 (extremely). Scores for each mood factor are obtained by summing the responses for each adjective defining the factor. The POMS was normed on both psychiatric outpatients and college students. Its reliability and validity have been established (McNair et al., 1971).

Beck depression inventory-II

The BDI-II is a widely used 21-item self-report measure of depressive symptoms. Respondents rate the presence of depressive symptoms over the past 2 weeks on a scale of 0–3, with higher scores indicating more severe symptoms. Possible scores range from 0 to 63, with scores of 0–13 reflecting no or minimal depression, scores 14–19 indicative of mild depression, 20–28 indicative of moderate depression and scores above 29 reflecting severe depression. The BDI-II has been shown to have good reliability and validity (Beck et al., 1996) and is used across a broad range of patient populations.

Statistical analysis

This study relied primarily upon descriptive statistics and t-test comparisons. A significance level of P < 0.05 was adopted for all comparisons. All statistical analyses were performed utilizing the PASW Statistical Software Package, version 18.

Results

Clinical status

The demographic characteristics of the candidate donors are presented in Table I. While all candidate donors were euthymic based upon results of structured clinical intake interview, nearly one-quarter (22.2%) candidate donors reported a history of major depressive disorder (MDD). One candidate donor reported that she had previously been hospitalized for suicidal ideation, and another reported having previously made a suicide attempt. All candidate donors who reported a history of MDD had received treatment for their depressive symptoms. More than half (58%) reported that they had received antidepressant medication as part of their treatment, while the remainder had received psychotherapy. None of the candidate donors reported a history of anxiety disorders.

Just over one-quarter (28.6%) of the women reported a history of emotional trauma or loss in their family of origin, including 3 women who reported alcoholism or other substance abuse in their family of origin, 2 women who reported a history of abuse (emotional/physical/sexual), 11 who reported their parents had been divorced and 4 who reported a death in their family of origin. Almost one-quarter (22.5%) reported that they had an abortion prior to presenting as a potential oocyte donor.

There was no significant difference between directed and anonymous donors in the rate of past episodes of MDD. Nine out of 40 directed donors reported a history of MDD (22.5%), while 5 out of 23 anonymous donors reported a history of MDD (21.7%). The chi-square statistic for this comparison was not significant ($\chi^2 (1) = 0.005, P = 0.944$).
Mean scores for each of the six POMS subscales are presented in Table II, compared with the corresponding scores from the POMS normative sample of college women (McNair et al., 1971). We used one-sample $t$-tests to compare the means of this sample’s POMS scores to those presented in the POMS manual for college-aged women. Candidate donors showed statistically significantly lower scores on all five negative mood subscales: tension–anxiety ($P = .000$); depression–dejection, ($P < .0005$); anger–hostility ($P < .0005$); fatigue–inertia ($P < .0005$) and confusion–bewilderment ($P < .0005$). They also showed significantly higher scores on the positive mood subscale (vigor–activity: $P = .009$). These scores were not suggestive of any type of current mood disturbance. Mean scores for the BDI-II are also presented in Table II, compared with the corresponding scores from the BDI-II normative sample of college students (Beck et al., 1996). Again, the mean scores from this sample were compared with the BDI-II normative sample of college women. Total scores on the BDI were significantly lower than those in the BDI-II sample of college students ($P < .0005$) and were not indicative of current depression.

### Discussion

This study adds to the literature regarding the clinical status of candidate oocyte donors and provides further information regarding important variables in donor evaluations. The main finding from this study is that oocyte donor candidates had a higher rate of previous major depressive episodes than the general population (Kessler et al., 1993), despite reporting very few current mood symptoms. Existing studies of donor candidates did not specifically report rates of previous major depressive episodes, although they did indicate outpatient counseling rates of 24–34% (Schover et al., 1991; Klock et al., 1999).

Schover et al. (1991) reported that 64% of their sample of 45 donor candidates had a history of mild depressive or anxiety symptoms, but this did not include rates of DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition), psychiatric diagnoses. Klock et al. (1999) reported that 10% of their sample had been on psychoactive drugs, but the type of drug used and DSM psychiatric diagnoses were not reported.

In our sample of candidate donors, almost one-quarter (22.2%) reported a history of MDD. By comparison, the National Comorbidity Study reported a 12-month prevalence rate of MDD among women.

### Psychometric scores for the BDI-II

<table>
<thead>
<tr>
<th>POMS subscale scores</th>
<th>Candidate oocyte donors ($n = 28$)</th>
<th>POMS normative sample (college women) ($n = 516$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Tension–anxiety</td>
<td>0.8</td>
<td>3.1</td>
</tr>
<tr>
<td>Depression–dejection</td>
<td>1.6</td>
<td>2.3</td>
</tr>
<tr>
<td>Anger–hostility</td>
<td>2.3</td>
<td>3.1</td>
</tr>
<tr>
<td>Fatigue–inertia</td>
<td>2.6</td>
<td>2.4</td>
</tr>
<tr>
<td>Confusion–bewilderment</td>
<td>1.5</td>
<td>2.6</td>
</tr>
<tr>
<td>Vigor–activity</td>
<td>18.9</td>
<td>5.3</td>
</tr>
</tbody>
</table>

### Total score

<table>
<thead>
<tr>
<th>BDI-II</th>
<th>Candidate oocyte donors ($n = 28$)</th>
<th>BDI-II normative sample of college students ($n = 120$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Total score</td>
<td>1.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Vigor–activity is a positive mood state, with higher scores indicating that the subject endorsed feeling higher levels of energy and ebullience.
studies have suggested that oocyte donors frequently under-report minimized symptoms to maintain eligibility for donation. Other risk for mood disturbance raises the question of whether candidates of MDD have increased risk for symptoms with the hormonal studies have specifically investigated whether women with a history scores reported by college students (McNair et al., 1971). The mean BDI-II scores also indicated a lack of depressive symptoms in this group of women, and again, the mean score was significantly lower than reported by Beck in his normative sample of college students (Beck et al., 1996). As assessed by clinical intake interview, none of the women endorsed current mood symptoms or reported being on an antidepressant or participating in psychotherapy, and none were diagnosed as currently suffering a depressive disorder. These findings are also interesting given point prevalence incidences of depressive disorders (Kessler, 2002), and the high recurrence rate of mood disorders (Kessler et al., 1993). Point prevalence of current major depression has been found to be ~2–4% for all adults in the general population, while it is estimated that up to 80% of individuals who experience a major depressive episode will experience recurrent episodes (Kessler, 2002).

This low rate of current mood symptoms in a group at an elevated risk for mood disturbance raises the question of whether candidates minimized symptoms to maintain eligibility for donation. Other studies have suggested that oocyte donors frequently under-report psychiatric symptoms (Schover et al., 1991; Lessor et al., 1993; Klock et al., 1999), and that on the Minnesota Multiphasic Personality Inventory (MMPI)-2 profiles, women who were accepted as oocyte donors tended to score highly on scales that measure under-reporting of symptoms and positive impression management (Klock et al., 1999). While the MMPI-2 is an informative tool, it is not currently required for donor evaluations and it is not trivial in its administration, requiring a trained psychologist and significant time for testing and scoring results. A shorter version, the MMPI-2-RF (Ben-Porath and Tellegen, 2008), may be an adequate alternative. In light of these findings, use of a measure of social desirability, such as the Marlowe Crowne Social Desirability Scale (Crowne and Marlowe, 1960), might be a useful adjunct to psychometric testing for candidate oocyte donors. The risk for under-reporting symptoms on a psychometric test further supports the importance of a detailed clinical interview for oocyte donor candidates. In an interview, subler aspects of depressive disorders, such as psychomotor retardation or affective blunting, can be observed and this non-verbal information can provide further diagnostic information.

The affective disorder history of oocyte donors is extremely important to clarify for two main reasons: the potential for ovarian stimulation medications to induce or exacerbate mood symptoms, and the genetic transmission of risk for mood disorders. Ovarian stimulation medications have been associated with mood symptoms, including irritability, mood instability, and mania and psychosis (Cashman and Sheppard, 1982; Altmark et al., 1987; Oyffe et al., 1997; Siedentopf et al., 1997; Parikh and Liskow, 2007; Habreich, 2010). To date, no studies have specifically investigated whether women with a history of MDD have increased risk for symptoms with the hormonal changes associated with ovarian stimulation medications, although several case reports have suggested that a prior mood disturbance may be a predisposing factor (Altmark et al., 1987; Oyffe et al., 1997; Parikh and Liskow, 2007). A growing body of literature highlights the important role of hormonal changes in destabilizing mood in women with a history of premenstrual dysphoric disorder, post-partum depression and bipolar disorder (Schmidt et al., 1998; Bloch et al., 2000; Habreich, 2010; Maki et al., 2010). It is recommended that the clinical interview for oocyte donors be expanded to emphasize investigation of mood and anxiety symptoms during previous times of hormonal change, such as exposure to oral contraceptives, premenstrually, during pregnancy, or post-partum.

Current ASRM guidelines recommend that donors who are excluded be counseled regarding the reasons, and if appropriate, offered referral, but the guidelines do not provide recommendations regarding follow-up of either excluded or non-excluded donors. Very few follow-up studies of oocyte donors exist, and most of the follow-up literature has explored only the donors’ attitudes toward donation (Purewal and van den Akker, 2009). Only one retrospective study reported donors’ psychological experiences during the donation cycle, and they found that while 7.5% of women were aware of the possibility of mood changes and irritability, the actual experience was in fact more common, affecting 15% of women (Kenny and McGowan, 2010). Future prospective studies are needed to clarify the prevalence of mood and anxiety symptoms during the oocyte donation process in general, and in donors with a history of hormone sensitivity in particular.

Finally, it is recognized that MDD is a moderately heritable disorder. According to twin studies, heritability is ~40–50%, and adoption studies have provided support for a genetic contribution (Levinson, 2006). The heritability of bipolar spectrum disorders may be even higher: according to recent twin studies, heritability estimates range from 89 to 93% (Craddock et al., 2005). Since the available data are consistent with a role of genetic transmission of risk for mood disorders, screening for these disorders among potential oocyte donors is important. Since many people are not aware of parental diagnosis, a detailed psychiatric history by an experienced clinician is extremely important for gathering information about parental behaviors that may suggest bipolar disorder or schizophrenia. Furthermore, it is recommended that the clinical interview be supported by psychometric testing that investigates the validity of the candidate’s responses (Reh et al., 2010). Although measures such as the MMPI-2 may be recommended as part of the screening process, they will not be utilized in all settings owing to time constraints in administering and interpreting the results. Nonetheless, there is significant value in supplementing clinical history with empirically validated psychometric tests that have the ability to capture under-reporting of symptoms and a tendency to engage in self-favorable descriptions.

**Limitations**

There are a number of limitations in our study which warrant caution in interpreting these results. First, this article reports only on the findings from the psychiatric screening interview. It is not an outcome study and does not include data regarding whether the candidate donor was accepted for donation. Second, the sample size is small and although it reflects reproductive endocrinology and infertility practices in a university setting, larger studies are needed. Finally, reported...
discrepancy between self-report and objective evaluation could be a result of other psychological differences in motivation of candidate donors, unexplored in the current report. However, results support recent studies emphasizing the need for detailed medical and psychiatric assessment of oocyte donors (Reh et al., 2010) and suggest that further longitudinal follow-up studies of this potentially at-risk population are warranted.

**Summary**

Comprehensive psychiatric evaluation of potential oocyte donors by trained psychiatric or psychological professionals is important, given the potential risks of the oocyte donation process. The psychiatric histories of oocyte donors should include a detailed assessment of past mood and anxiety disorders, specifically focusing on sensitivity to mood destabilization during times of hormonal change. Current mood states should be evaluated with both objective and subjective measures and should be accompanied by tests that examine social desirability and trends toward minimizing symptoms.

**Authors’ roles**

K.E.W. was responsible for completing the oocyte donor interviews, conceptualizing the study design, and writing of the manuscript. P.G.S. was responsible for the statistical analysis of all data, writing up results and revision of the manuscript. L.M.W. was responsible for the recruitment and medical evaluation of donor candidates, study conceptualization and critical revision of the paper. N.L.R. was involved in the interpretation of results and critical revision of the manuscript.

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**Conflict of interest:** K.E.W., P.S. and L.M.W. report no conflicts of interest related to this manuscript. N.L.R. is currently on advisory boards for Pfizer.

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**References**


Levinson DF. The genetics of depression: a review. *Biol Psychiatry* 2006;60:84–92.


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