DSMV: The Perinatal Onset Specifier for Mood Disorders

Dr Ian Jones
Senior Lecturer in Perinatal Psychiatry and Consultant Perinatal Psychiatrist.
Cardiff University, UK.

Background

The link between childbirth and affective disorders has been recognised for many hundreds of years. It is also clear that episodes of mood disorder occurring at this time are of great clinical and public health importance with suicide a leading cause of maternal death in the developed world (CEMACH, 2007). The nosology of perinatal episodes, however, is controversial and has lead to confusion in both clinical practice and research. I will here consider the relevant literature and make recommendations for DSM-V focussing on the issue of the postpartum onset specifier.

Bipolar disorder

For episodes of severe affective psychosis, and for bipolar episodes in particular, there is very clear evidence of a specific relationship to childbirth (Jones and Craddock, 2005). In a large study employing the Danish admission and birth registries that examined over 600,000 pregnancies and postpartum periods, women were over 23 times more likely to be admitted with an episode of Bipolar disorder in the first postpartum month (RR=23.33, 95% C.I.s 11.52 - 47.24) (Munk-Olsen et al, 2006). A previous history of admission with bipolar disorder was associated with an even larger increased risk of admission following pregnancy (RR=37.22, 95% CI's 13.58 – 102.4) (Munk-Olsen et al, 2008 and in press). Another recent Scandinavian register study that found a lower risk to bipolar women (Harlow et al, 2006) was methodologically flawed, including a large number of unipolar disorder cases in the bipolar group (discussed in Jones et al, 2008).

Bipolar women have at least a 1 in 4 risk of suffering a severe recurrence following delivery (Jones and Craddock, 2001). Bipolar women with a previous history of a severe postpartum episode (postpartum /puerperal psychosis) and bipolar women with a family history of postpartum psychosis are at particularly high risk with greater than 1 in 2 deliveries affected (Jones and Craddock, 2001; Robertson et al, 2005). For postpartum episodes on the bipolar spectrum there is a characteristic and close temporal relationship to childbirth. In a study of 111 episodes of postpartum psychosis, 97% of women retrospectively reported the onset of symptoms within the first two postpartum weeks with the majority on days 1-3 (Heron et al, 2007). Familial factors have been implicated in the vulnerability to postpartum triggering of bipolar episodes (Jones and Craddock, 2001) with evidence from linkage studies indicating the possible location of susceptibility genes (Jones et al, 2007).

Despite few studies in this area, It is also likely that the presentation of bipolar episodes in the postpartum period show some differences, with mixed episodes, dysphoric mania, a rapidly changing "kalaedoscopic" clinical presentation, and perplexity and confusion more prominent (Reviewed in Brockington 1996). There is therefore a clear justification for recognising this

very strong relationship between bipolar spectrum disorders and childbirth in the classification systems.

Major Depression

For non-psychotic episodes of major depression a specific relationship to childbirth has been challenged. In contrast to bipolar disorder, a number of controlled studies have not found depression to be more common in the postpartum period (e.g. Cooper *et al*, 1988; O'Hara *et al*, 1990; Cox *et al*, 1993). However, there are methodological problems with studies in this area in determining which comparison groups should be used. The work of Munk-Olsen and colleagues with the Danish psychiatric admission and birth registries have demonstrated what they term a "selection into parenthood", that is women who become mothers are a group at lower risk for psychiatric disorders (Munk-Olsen et al, 2006). Analyses that address this issue do reveal an increased risk of depression in the postpartum. The Danish study found an over three fold increased risk of admission with unipolar depression on postpartum days 31- 60 (RR=3.53, 95% CIs 2.37-5.05) (Munk-Olsen et al, 2006). In addition, Eberhard-Gran and colleagues (2002) found that although rates of depression appeared to be lower in the postpartum period, when other risk factors for depression were controlled for, the risk was actually two fold higher than at other times.

There is also support for a specific relationship between childbirth and depression in aetiological studies. Despite negative results from studies examining the absolute level of various hormones, it has been suggested that women with postpartum depression show an abnormal response to the normal physiological changes of pregnancy and empirical data has been reported in support of this hypothesis (Bloch *et al*, 2000). A recent study has also found significant evidence that a vulnerability to postpartum episodes of depression is familial (Forty et al, 2006).

With regard to the phenomenology of episodes of depression in the postpartum period there is a lack of consistency in the literature. A number of reports identified differences in the clinical presentation of postnatal and non-postnatal depression (Pitt, 1968; Whiffen & Gotlib, 1993; Eberherd-Gran *et al*, 2003) but most studies find the clinical presentation is not distinctive (Cooper et al, 2007; Cooper *et al*, 1988; Whiffen, 1992; Evans *et al*, 2001).

Perinatal episodes in the classification systems

There is clear evidence then, supporting a specific relationship with childbirth for mood disorders on the bipolar spectrum and, to a lesser extent, evidence that episodes of non-psychotic major depression are also associated with childbirth. Despite not being a diagnostic category in either DSM-IV or ICD10, postpartum (postnatal in the UK) depression (PPD) and postpartum (puerperal) psychosis (PP) have remained in common use by the lay public and health professionals. There are however, a number of problems with their continued prominence, particularly the use of PPD to refer to the whole range of psychological distress following childbirth, from the mild and transient "baby blues" through to episodes of severe and potentially devastating affective

psychosis. This has lead to the confidential enquiries in the UK to recommend that the terms PND/PPD not be employed, as they are too wide to have any useful meaning (CEMACH, 2007).

The weight of evidence does not support PPD and PP as separate nosological entities and I support the approach of diagnosing episodes of mood disorder in relation to childbirth in the normal categories of the mood disorder rubric. There are distinct benefits, however, in flagging episodes in relation to childbirth and I support the retention of the postpartum onset specifier in DSMV. The main advantage is that the link to childbirth carries prognostic information with regard to the risk following future pregnancies. For bipolar women with a severe postpartum episode, there is greater than 60% risk of a severe recurrence following a further pregnancy, compared to a risk of around 25% for bipolar women who have not experienced a postpartum episode (Robertson et al, 2005). A history of unipolar depression clearly increases risk for postpartum depression (O'Hara and Swain, 1996) and there is also evidence to suggest a specific vulnerability to postpartum triggering in some women (Cooper and Murray, 1995; Forty et al, 2006). Having an episode of depression linked to childbirth, therefore, has implications for future pregnancies and identifies women at a particular risk – a higher risk than for women with merely a history of depression at other times.

There are issues, however, with regard to how the specifier is employed.

Should the onset specifier cover pregnancy?
There are a number of options: a separate specifier for pregnancy and the postpartum; a perinatal onset specifier to include onsets in pregnancy and the postpartum; or finally, maintaining the specifier for postpartum onsets only. Depression clearly occurs in pregnancy and self report questionnaire studies in the general population suggest that depressive symptoms are as common as in the postpartum period (e.g. Ferguson et al, 1996). For more severe episodes of major depression however, the risk appears to be considerably lower in pregnancy. In the large Danish registry studies, for example, the RR for admission with unipolar depression in pregnancy was 0.44 (95% CI 0.31-0.62) compared to a RR of 3.53 in the postpartum (95% CI 2.47-5.05) (Munk-Olsen et al, 2006). For bipolar disorder, the increased risk in the postpartum period is even more impressive (pregnancy RR=0.19 (0.04-0.86), first postpartum month RR=23.33 (11.52-47.42). Although the Danish study concerns admission rather than strictly episode onset and it is possible that some episodes resulting in postpartum admissions began in pregnancy, this is unlikely to be a frequent occurrence. Studies of postpartum psychosis show a very characteristic onset in the first postpartum weeks (Heron et al, 2007). For these reasons I believe the literature points to a specific relationship with the postpartum and would support maintaining the specifier for postpartum onsets.

What period following childbirth should the specifier cover?
The difficulty in addressing this question results from a very different pattern of postpartum onsets in bipolar and unipolar disorder. In bipolar disorder there is a clear clustering of onsets in the immediate puerperium. In a study of 111

severe postpartum bipolar episodes over 97% had their onset within the first two postpartum weeks (Heron et al, 2007; Heron et al, 2008). In the Danish data, the very high relative risk of admission in the first postpartum month (RR=23) fell off very quickly (RR=6.3 for month 2) and was not raised for onsets after 2 months (Munk-Olsen et al, 2006). Onsets of unipolar depression are more spread out in the postpartum period. In the Danish data, the increased risk of admission with unipolar disorders persisted through the first 5 months postpartum and was at its maximum in the second postpartum month (Munk-Olsen et al, 2006). Further evidence comes from the study of Forty and colleagues (2006) which examined the familiality of postpartum triggering in pairs of sisters with recurrent major depression. A range of definitions of postpartum onset were tested from one week to 6 months following delivery with the evidence for familiality maximising for definitions of postpartum onset in the first 6 – 8 weeks following delivery (Figure 1.).

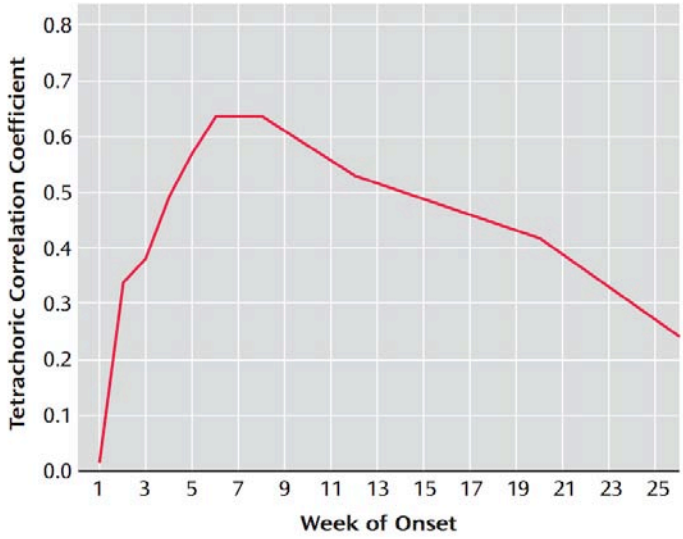

Figure 1. Evidence of familiality of postpartum triggering for various definitions of postpartum onset in parous sisters with unipolar disorder.

In everyday use, PPD is used to refer to episodes with onset up to 6 months following delivery and from the evidence above we can conclude that for unipolar depression a 4 week specifier is too restrictive. For the onset of bipolar episodes the current cut off may be appropriate but the option of multiple specifiers for BP and UP episodes is a more complex solution that is unlikely to be acceptable. If multiple specifiers were employed, a six month duration for depressive episodes would be preferable compared to a one month duration for manic or mixed episodes. If one specifier were retained, I would recommend extending the criteria to episodes with onsets within 2 months of delivery.

Summary of recommendations

It is difficult to make specific recommendations when the final structure of DSM-V is unknown. It is also not possible to deal with major depression in

isolation as how postpartum episodes are dealt with has implications for bipolar disorder and there are important distinctions across the mood disorder spectrum. However, based on the current state of the literature described above I make four recommendations:

1. Retain the onset specifier in the mood disorders rubric.
2. Retain the specifier for postpartum onsets.
3. If different specifiers, keep duration to 4 weeks for manic or mixed episodes and extend the duration to 6 months for depressive episodes.
4. If one specifier, extend the criteria to episodes with onsets within 2 months of delivery.

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