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Obsessive-compulsive disorder in the perinatal period: Epidemiology, phenomenology, pathogenesis, and treatment

Álvaro Frías[1]*, Carolina Palma[1], Francisco Barón[1], Paloma Varela[2], Ana Álvarez[2] and Ana Salvador[2]

[1] *FPCEE Blanquerna (Ramon-Llull University) (Spain)*
[2] *Department of Psychiatry. (Hospital of Mataró) (Spain)*

Título: Trastorno obsesivo-compulsivo durante el período perinatal: epidemiología, fenomenología, etiopatogenia y tratamiento.
Resumen: El objetivo de la presente revisión teórica es describir los principales hallazgos e investigaciones sobre el trastorno obsesivo-compulsivo (TOC) durante el período perinatal. Por una parte, los estudios epidemiológicos señalan que en esta etapa aumenta el riesgo de debut y/o exacerbación del TOC, especialmente en el puerperio. A nivel fenomenológico, predominan las obsesiones agresivas y de contaminación relacionadas con la figura del feto o neonato. En cuanto a su etiopatogenia, existen evidencias indirectas para postular la participación de variables neuroendocrinas (p.e. esteroides gonadales femeninos y oxitocina) y cognitivo-conductuales (p.e. hiperresponsabilidad, sobreestimación de la amenaza y control mental), siendo necesaria una mayor contrastación empírica de estos correlatos y/o factores de vulnerabilidad específicos. En el ámbito interventivo, se carece de ensayos clínicos aleatorizados con grupo control adaptados a las características idiosincrásicas de este subgrupo de sujetos con TOC. Así mismo, se destaca el papel de la terapia cognitivo-conductual (TCC) en el marco de la prevención primaria selectiva.
Palabras clave: Trastorno obsesivo-compulsivo; período perinatal; prevención primaria; terapia cognitivo-conductual; estudio teórico.

Abstract: The aim of this review is to describe the main theoretical findings and research conclusions about obsessive-compulsive disorder (OCD) in the perinatal period. On one hand, epidemiological studies show that the risk of OCD onset and/or exacerbation could increase in this period, particularly in the puerperium. Phenomenologically, in this stage aggressive and contamination obsessions are very common and are related to the fetus or newborn. On the other hand, regarding OCD pathogenesis in this period, there is indirect evidence to suggest the participation of neuroendocrine (e.g. female gonadal steroids and oxytocin) and cognitive behavioural variables (e.g. hyper-responsibility, threat overestimation, and mental control). In terms of research, more empirical studies are needed to contrast these specific vulnerability factors. Moreover, no empirically validated psychotherapeutic treatments (controlled trials) adapted to this OCD subgroup were found, although some studies highlight the role of cognitive behavioural therapy (CBT) as an effective intervention in the context of selective primary prevention.
Key words: Obsessive-compulsive disorder; perinatal period; primary prevention; cognitive behavioural therapy; theoretical study.

Introduction

The perinatal period is a stage that involves many hormonal and psychosocial changes that synergistically merge throughout this evolutionary process between pregnancy and postnatal period (or puerperium). Since the last three decades in the 20th century, some empirical evidence has associated this biopsychosocial process with the onset, relapse or exacerbation of different mental disorders in women, with much research focusing on the onset of depressive episodes and psychotic symptoms during the puerperium (Hudak & Wisner, 2012; Spinelli, 2009; Steiner, Dunn, & Bom, 2003). In this general context, anxious psychopathology did not arouse much clinical interest until the mid-1990s, when incipient literature started to develop with the assessment of obsessive-compulsive disorder being the main focus of attention (Matthey, Barnett, Howie, & Kavanagh, 2003; Ross & McLean, 2006).

The study of this subgroup of women with perinatal obsessive-compulsive disorder (pOCD) is not only significant from a psychopathological and epidemiological point of view, but is also a relevant variable at a functional level as egodystonic thoughts may condition the bond between mother and child (Brandes, Soares, & Cohen, 2004; Mavrogiorgou, Illes & Juckel, 2011). These data are even more significant if we consider that mothers with obsessions related to their children (e.g., aggressive intrusions) usually hide or minimize these symptoms for fear of being stigmatized, which results in less treatment demands (underdiagnosis), and in a higher risk for the disorder to become chronic (Abramowitz, Schwartz, Moore, & Luenzmann, 2003; Rosso, Bechon, Bogetto, & Maina, 2012; Uguz, Kaya, Sahingoz, Cilli, & Akman, 2008). In this connection, it is important to remark that OCD is often a very comorbid disorder with depression, being usually OCD the antecedent. In this context, there is abundant scientific literature that emphasizes the impact of mental disorders in general and particularly of OCD in negative parenting styles and behaviors. Thus, it is another reason to identify and treat early this disorder during the perinatal period (Black, Gaffney, Schlosser, & Gabel, 2003; Mann & Gregoire, 2000; Storch et al., 2007). There are others studies that suggest it is necessary the differencial diagnosis in the perinatal period and the early initiation of an adequate therapy (Mavrogiorgou et al., 2011).

Objectives and method

From this approach, this review has the main objective to present an updated framework of the major breakthroughs in the study of pOCD. More specifically, it aims at improving the comprehension of clinicians and experts about (1) clinical characteristics, (2) risk factors, and (3) treatment of this psychopathology during the perinatal period. Compared to other recent theoretical reviews (Mavrogiorgou et al., 2011; McGuinness, Blissett, & Jones, 2011), provides last advances in both treatment and neuroendocrine pathogene-

*** Dirección para correspondencia [Correspondence address]:**
Álvaro Frías Ibáñez. Servicio de Psiquiatría. Hospital de Mataró. Ctra. Cirera s/n . 08304 Mataró, Barcelona (Spain).
E-mail: afrias@csdm.cat

sis of pOCD. Literature research was carried out through PubMed and PsycINFO from 1980 to November 2012. The descriptors used were "*OCD*", "*obsessive-compulsive*", "*obsessive*", "*compulsive*", "*perinatal*", "*puerperium*", "*postpartum*" and "*pregnancy*". Seventy articles were selected in connection with this purpose, including theoretical (9), quasi-experimental (13) and descriptive articles (48). Findings were classified according to the following sections: epidemiology, phenomenology, pathogenesis, and treatment.

Epidemiology

Those studies that assess the presence of obsessive-compulsive symptoms during the perinatal period have focused on either assessing *de novo* OCD throughout pregnancy and/or puerperium (incidence) or quantifying its frequency regardless of the subject's having this psychopathology before the perinatal period (prevalence). With this aim, prospective assessment of gynaecological samples during pregnancy and/or postpartum was used, as well as retrospective analysis of psychiatric female patients with OCD. Additionally, there are other methodological divergences that condition the generalization of findings, mainly discrepancies concerning the determination of assessment intervals during pregnancy (e.g., completed gestation versus third trimester) and postpartum/puerperium (e.g., 6 vs. 26 weeks) (Chaudron & Nirodi, 2010; Uguz et al., 2007b; Wenzel, Haugen, Jackson, & Brendle, 2005).

Apart from these considerations, epidemiological studies show that the prevalence of OCD during pregnancy is estimated to be in a range between 0.2% and 3.5% (Andersson et al., 2003; Sutter, Giaconne, Glatigny, & Verdoux 2004; Uguz et al., 2007a; Zar, Wijma, & Wijma, 2002), with an increase of up to 2.3-9% in the postnatal period (Wenzel et al., 2005; Zambaldi et al., 2009). This difference has to be considered taking into account that its life prevalence in general population is 2.5-3.5% (Fontenelle, Mendlowicz, & Versiana, 2006; Kessler, Chiu, Demler, Merikangas, & Walters, 2005; McGuinness et al., 2011). Moreover, the incidence of this mental pathology during pregnancy and puerperium has similar results in both stages, with ranges between 2.2-15.4% and between 2.3-14.1%, respectively (Chaudron & Nirodi, 2010; Forray, Focseneanu, Pittman, & McDougle, 2010; Labad et al., 2005; Uguz, Akman, Kaya, & Cilli, 2007; Williams & Koran, 1997; Zambaldi et al., 2009). As a whole, these incidence data highlight that the proportion of new OCD cases during the entire perinatal period is estimated at around 5-30% of samples assessed (Forray et al., 2010; Neziroglu, Anemone, & Yaryura-Tobias, 1992).

Additionally, another series of longitudinal studies have been designed with the aim of assessing the course of this psychopathology throughout the entire perinatal period, with a selection of gynaecological patients with its onset during their gestational stage. In general, a psychopathological improvement has been observed during pregnancy in 14-22% of cases, with an exacerbation of the disorder in 8-34.1% of patients (Forray et al., 2010; Labad et al., 2005; Vulink, Denys, Bus, & Westenberg 2006; Williams & Koran, 1997). With regard to the puerperal period, there is a worsening in the obsessive-compulsive condition in 29-50% of women (Labad et al., 2005; Williams & Koran, 1997).

In conclusion, the perinatal period is a stage that increases the risk of onset or exacerbation of OCD, particularly in the puerperium. When trying to assess the prevalence of pOCD, it is important to consider whether intrusive thoughts (particularly aggressive ones) are better explained due to the presence of postpartum depression (Abramowitz et al., 2010; Jennings, Ross, Popper, & Elmore, 1999; Wisner, Peindl, Gigliotti, & Hanusa, 1999).

Phenomenology

The phenomenological analysis of intrusive thoughts in patients with pOCD has been carried out from two divergent approaches. On the one hand, its pathoplasty has been explained from a dimensional paradigm, which involves all the women in the perinatal period in different amounts or to different extents. On the other hand, a category method has been proposed by assessing the qualitative differences in comparison to other OCD patients whose course is not conditioned by this perinatal period.

From the first approach, much research has found that the presence of intrusive thoughts during pregnancy and puerperium is a relatively common phenomenon, with 49-69% of women being affected in the perinatal period (Abramowitz et al., 2003; Leckman et al., 1999). The nature of this condition is usually related to the newborn, mainly through aggressive content involving accidental or deliberate harm towards them. This symptom is unsteady, not very intense, and causes scarce interference. From an evolutionary point of view, this high prevalence sets out its possible former adaptive value, as it would alert the mother to the potential dangers that their child might be exposed to when living conditions were not as safe as at present (Ross & McLean, 2006). In this dimensional framework, there are a proportion of women, whose symptoms are hypertrophied, reaching an intensity and frequency beyond the clinical threshold.

From a category perspective, there have been scarce comparative studies between patients with pOCD and with "non-perinatal" OCD (npOCD), with a higher frequency of aggressive and/or contamination obsessions in the first subgroup (Forray et al., 2010; Uguz et al., 2007). These data are more significant if we consider that, in the context of all the population with OCD, aggressive and contamination obsessions are also predominant (Mataix-Cols et al., 2002). At a qualitative level, research with samples with pOCD shows that during pregnancy there is a prevalence of contamination obsessions concerning the fetus, which usually results in cleaning rituals (Chelmow & Halfin, 1997; Kalra, Tandon, Trivedi, & Janca, 2005; Labad et al., 2010). On the other hand, during puerperium there is a higher frequency of ag-

gressive intrusions towards the infant, which predispose to them to (1) avoidant behaviours in the case of considering deliberate harm (e.g., killing the infant with a knife or throwing the baby's pram into the road) or (2) checking compulsions when an accidental harm or not related to the mother is considered (e.g., fear that the baby might drown while being bathed, or that a stranger might kidnap the infant) (Arnold, 1999; Sichel, Cohen, Dimmock, & Rosenbaum, 1993; Zambaldi et al., 2009). In this sense, there is a self-administered questionnaire expressly designed to assess these phenomena (Lord, Rieder, Hall, Soares, & Steiner, 2011).

In conclusion, the perinatal period is a stage that determines in itself the pathoplasty of OCD, as aggressive and contamination obsessions are related to the fetus or newborn (Rosso et al., 2012). Long-term (2-5 years) prospective studies are needed in order to determine whether patients with perinatal onset OCD develop later intrusions not linked to their children.

Pathogenesis

From the findings about the high prevalence and symptomatological specificity of pOCD, a line of research has been promoted to determine the pathogenesis of this disorder. In this context, 3 theoretical frameworks have been proposed to explain pOCD: sociobiological, neuroendocrine, and cognitive-behavioural. So far, none of these models has enough empirical validity to become an approach of reference.

Firstly, the sociobiological theory maintains that the genesis of pOCD lies in a greater reactivity or deregulation of the hypothalamic-pituitary-adrenal (HPA) axis as a response to stressful life events (Abramowitz et al., 2003; Maina, Albert, Bogetto, Vaschetto, & Ravizza, 1999). In this sense, some research has found that, although patients with pOCD have higher levels of cortisol and/or corticotropin that a healthy control group (Labad et al., 2011), they hardly show a higher production of adrenaline and/or cortisol in response to a stressful task (Lord, Hall, Soares, & Steiner, 2011; Lord, Steiner, Soares, Carew, & Hall, 2012). Moreover, these intergroup differences have no specificity as subjects with npOCD also show higher basal activity in the HPA axis than healthy control subjects (Gustafsson, Gustafsson, Ivarsson, & Nelson, 2008). With regard to this hypothesis, no comparative research has been carried out between pOCD and npOCD.

Concerning the neuroendocrine theory, a serotonergic deregulation is postulated due to fluctuations in female gonadal steroids during the perinatal period (Forray et al., 2010; Labad et al., 2005). Some indirect supports have been established to corroborate this model. On the one hand, the variability in the levels of estradiol and progesterone are known to affect the production of catecholamines and indolamines (Flaisher-Grinberg et al., 2009; Gardiner et al., 2004; McEwen, 2002; Thompson, 1999). On the other hand, women with pOCD (versus npOCD) have been found to show a worsening of this psychopathology during the premenstrual phase (Forray et al., 2010; Labad et al., 2005; Williams & Koran, 1997). Finally, patients with pOCD usually show greater comorbidity with major depressive disorder than healthy control subjects or patients with npOCD (Chaudron & Nirodi, 2010; Labad et al., 2005; Zambaldi et al., 2009). However, this finding has not been observed in all the studies (Forray et al., 2010), which should be considered taking into account the high comorbidity between major depression and OCD in the total group of obsessive patients (Rasmussen & Eisen, 1994). In another perspective, an additional neuroendocrine hypothesis deals with the role of oxytocin, a hormone the synthesis of which is increased during the third trimester of pregnancy and the puerperium with the aim of enhancing uterine contractions, milk production, and the mother role in general (Forray et al., 2010). In this sense, there are preliminary findings that show that, in contrast with healthy control subjects, subjects diagnosed with OCD show higher levels of this hormone in their cerebrospinal fluid (Leckman et al., 1994). As a whole, the two neuroendocrine hypotheses present the problem of a deficit in studies that have directly compared these hormone levels among gynaecological patients without OCD, pOCD and npOCD. Not only does this prevent from determining the presence of vulnerability factors during the perinatal period, but also their specificity in relation to other subjects with OCD.

Concerning the cognitive-behavioural model, the role of hyper-responsibility and overestimation of threat or danger is highlighted as intrapsychic factors that contribute to an inappropriate interpretation of normative intrusions in people exposed to a new life event as parenthood (Fairbrother & Abramowitz, 2007; Fairbrother & Woody, 2008). From this, the disorder is maintained through those coping mechanisms used to face intrusions (e.g., mental control, avoidant behaviours, compulsions) (Larsen et al., 2006). Indirect support has been obtained in favour of this hypothesis. Firstly, pOCD always occurs from the first pregnancy and is independent of the number of pregnancies (Forray et al., 2010). Secondly, there are case studies that confirm that OCD also occurs in some men that are going to be fathers (Abramowitz, Moore, Carmin, Wiegartz, & Purdon, 2001; Petribú, Eleuterio, Domínguez, Lima, & Ferrão, 2011). Finally, as mentioned before, intrusive thoughts during the perinatal period are a quasi-universal phenomenon and their pathoplasty is related to the fetus or the newborn (Leckman et al., 1999). Although this is a promising theory, no comparative research has been carried out to contrast the degree of hyper-responsibility in patients with pOCD, healthy control gynaecological subjects and/or women with npOCD. Likewise, it is still not clear whether obstetric complications (additional stressful agent) have some modulating role on the levels of hyper-responsibility. So far, some studies have found a higher risk of having pOCD in women with obstetric complications (Maina et al., 1999; Zambaldi et al., 2009), whereas other research dismisses this option (Forray et al., 2010; Labad et al., 2005; Uguz et al., 2007a). On the other

hand, it is known that cognitive behavioral framework includes the role of cultural factors in the symptomatic expression of TOC (e.g. compulsions such as cleaning and disinfection). Studies suggest that the onset form of OCD is related to cultural factors that operate on cognitive processes (Yorulmaz, Tülin, & Woody, 2009), most likely influenced by advertising related or recommendations by health professionals. However found no empirical studies on the influence of these factors on the onset of pOCD.

In conclusion, there is indirect and preliminary evidence to postulate the participation of neuroendocrine and cognitive-behavioural variables in the genesis of pOCD. Nevertheless, greater empirical contrast of these specific correlates and/or vulnerability factors, regardless of the aprioristic models proposed, is needed. Moreover, interdisciplinary research that tries to find out whether there is some kind of relationship among apparently divergent approaches (e.g., levels of oxytocin and degree of hyper-responsibility) should be promoted.

Treatment

A last incipient area of research is connected to interventions for patients with pOCD. The treatment of this psychopathology is extremely important both from a clinical and functional point of view. On the one hand, obsessive-compulsive symptoms tend to perpetuate in the mid term (a year) with the lack of therapeutic monitoring during postpartum (Rosso et al., 2012; Uguz, Kaya, Sahingoz, Cilli, & Akman 2008). On the other hand, they condition the mother-child bond, with the mother developing avoidant attachment in response to intrusive and egodystonic thoughts (Brandes et al., 2004; Chelmow & Halfin, 1997; Gezginc et al., 2008). Ultimately, the feelings of shame and stigmatization experienced by mothers lead to an underdiagnosis, thus limiting their access to therapeutic resources that could reverse this psychopathological and psychosocial evolution (McGuinness et al., 2011).

With regard to psychopharmacological interventions, those treatments empirically validated for general OCD population have traditionally been used, that is, antidepressants as first-line agents (Brandes et al., 2004; Hudak & Wisner, 2012). In this sense, there is an open clinical trial that confirms that the prescription of fluvoxamine (final dose 150-300 mg) significantly reduced the severity of pOCD in two thirds of the patients that completed the study three months after (Arnold, 1999). Likewise, in another open trial with women with refractory pOCD in antidepressant monotherapy, the incorporation of quetiapine (mean final dose 112.5 mg) was beneficial in three quarters of the women that completed the study 12 weeks after. Regardless of these results, in the specific case of women with pOCD, some peculiarity has to be highlighted when extrapolating these tools to this subgroup. The first, and most important, one is about the potential risks for the fetus or the newborn when using antidepressants (Alwan & Fiedman, 2009; Oberlander, Warburton, Misri, Aghajanian, & Hertzman 2006). Taking into account the cost-benefit ratio of their administration, there are many "hyper-responsible" women that decide to give up psychopharmacological therapy for this reason (Arnold, 1999). In this context, some authors consider cognitive behavioural therapy to be the treatment of choice for pOCD (McDonough & Kennedy, 2002).

With regard to psychotherapeutic interventions, treatments empirically validated in general population with OCD have been usually used, mainly cognitive behavioural therapy (CBT) (Rosa-Alcázar, Sánchez, Gómez, & Marín, 2008). As in psychotropic interventions, there is no clinical trial with control group where the efficiency of CBT has been assessed in patients with pOCD. Nevertheless, in some case studies it has been observed that the use of cognitive-behavioural techniques such as psychoeducation, exposure and response prevention, behavioural experiments, and cognitive restructuring, reduces this perinatal psychopathology, although the risk of relapse in the short term (3 months) is quite high (Christian & Storch, 2009). Likewise, there are other cases that show the maximization of therapeutic gains of this treatment through an intense intervention format (six 2-hour sessions for 2 weeks), monitored from the patient's own home. This implies the use of in vivo exposures in the presence of the newborn (Hudak & Wisner, 2012), as well as greater preservation of the mother role as the therapy takes less time outside home (Challacombe & Salkovskis, 2011). Being this a promising intervention format, its implementation by public mental health professionals is limited by their possibilities of action. This, together with the scarce demand for treatment by patients with pOCD, has brought up the suitability of focusing psychotherapeutic efforts on selective primary prevention, that is, guiding intervention towards those pregnant women with some risk factors for pOCD (e.g., moral thought-action fusion and/or hyper-responsibility). In this sense, there is a pilot study with a control group where an improvement in coping style (less need to control thoughts) and in the severity of mental intrusions has been observed in those patients in CBT (Timpano, Abramowitz, Mahaffey, Mitchell, & Schmidt, 2011).

In conclusion, there are no empirically validated treatments adapted to the idiosyncratic characteristics of patients with pOCD (Speisman, Storch, & Abramowitz, 2011). More knowledge about the specific vulnerability factors in this population is needed in order to apply preventive interventions to the most appropriate target groups.

Discussion and conclusions

This theoretical study has the aim of presenting an updated framework for the main empirical findings concerning the epidemiology, phenomenology, pathogenesis and treatment of OCD during the perinatal period. With regard to the first aspect, there is agreement in stating that this period is a critical stage in the development and/or exacerbation of this psychopathology, mainly during the puerperium (or postpar-

tum). At a phenomenological level, there is a predominance of contamination obsessions during pregnancy and aggressive intrusions in the puerperium, with both being related to the fetus or the newborn (Leckman et al., 1999; Misri & Kristin, 2007). Concerning its pathogenesis, two models have been proposed with indirect evidence in their favour (cognitive-behavioural and neuroendocrine). Finally, in the treatment of this psychopathology, the use of cognitive behavioural psychotherapy stands out as a first-line intervention, particularly in the framework of selective primary prevention.

With regard to limitations observed, firstly there are remarkable methodological deficiencies that condition the generalization and validity of the epidemiological findings, that is: (1) reduced sample sizes, (2) heterogeneity in the kind of population selected (gynaecological samples versus OCD), (3) discrepancies in intervals assessed during pregnancy and/or puerperium, (4) no examination of possible concomitant depressive symptoms (differential diagnosis), and (5) use of retrospective designs (Speisman et al., 2011). With the aim of optimizing these deficiencies, it would be advisable to carry out prospective studies with gynaecological samples, which were assessed from the beginning of pregnancy and up to 6 months after delivery. A simple examination method would be to use the Perinatal Obsessive-Compulsive Scale (Lord et al., 2011), which could be used in the framework of regular visits that patients have with gynaecologists and/or primary care clinicians.

Another relevant limitation of this study on pOCD is the lack of empirical evidence on the potential associated vulnerability factors. In this sense, it is necessary to carry out comparative research where intergroup differences are assessed among pOCD, npOCD and gynaecological patients without OCD. On the one hand, at the neuroendocrine level, no study has been carried out that monitors and contrasts the levels of female steroids and/or oxytocin (Costas et al., 2010). As for the cognitive behavioural model, there have neither been comparative studies regarding the levels of hyper-responsibility (McGuiness et al., 2011). Likewise, pathogenetic research presents a deficit in interdisciplinary approaches, with a need to assess whether there is some kind of association between neuroendocrine and cognitive-behavioural variables.

With regard to the field of intervention, research is at an embryonic state despite the limitations to extrapolate the use of therapies validated in general OCD population to this subgroup (Hudak & Wisner, 2012). On the one hand, the use of psychodrugs poses potential risks for the fetus or the newborn, which increases reticence in many women with pOCD. Nevertheless, when these patients do not respond to psychological therapy, the psychotropic option emerges as the necessary line of action, which leads to their regular monitoring in perinatal psychiatry units. Concerning CBT, there are serious difficulties to adapt efficient intervention formats (long, regular and family-based in vivo exposures) in the clinical practice of professionals in the National Health Care System. This, together with the low demand of treatment by these patients, has to guide psychotherapeutic research towards selective primary prevention, which could be carried out through group sessions in primary care centres (Misri & Kristin, 2007; Timpano et al., 2011). However, for these interventions to be efficient, the priority has to be to determine the vulnerability factors specifically associated to pOCD.

Finally, the lack of long-term prospective studies is worth highlighting (Uguz et al., 2008), with an assessment of (1) the course of this obsessive-compulsive psychopathology after the puerperium (e.g., does the pathoplasty and/or severity of OCD change?), as well as relevant variables such as (2) degree of psychosocial dysfunctionality (e.g., mother-child bond), (3) self-esteem (stigmatization), (4) adherence to treatment, and (5) association with depressive symptoms. Considering evidence available about this subgroup of OCD patients, and with a view of optimizing their research and (under) diagnosis, it would be advisable to include an evolutionary criterion called "postpartum onset" when classifying this disorder in nosological manuals of reference.

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