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Research report

Seafood consumption, the DHA content of mothers' milk and prevalence rates of postpartum depression: a cross-national, ecological analysis

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Abstract

Background: Mothers selectively transfer docosahexaenoic acid (DHA) to their fetuses to support optimal neurological development during pregnancy. Without sufficient dietary intake, mothers become depleted of DHA and may increase their risk of suffering major depressive symptoms in the postpartum period. We postulated that the DHA content of mothers' milk and seafood consumption would both predict prevalence rates of postpartum depression across countries. *Methods*: Published prevalence data for postpartum depression were included that used the Edinburgh Postpartum Depression Scale ($n = 14\,532$ subjects in 41 studies). These data were compared to the DHA, eicosapentaenoic acid (EPA) and arachidonic acid (AA) content in mothers' milk and to seafood consumption rates in published reports from 23 countries. *Results*: Higher concentrations of DHA in mothers' milk ($r = -0.84$, $p < 0.0001$, $n = 16$ countries) and greater seafood consumption ($r = -0.81$, $p < 0.0001$, $n = 22$ countries) both predicted lower prevalence rates of postpartum depression in simple and logarithmic models, respectively. The AA and EPA content of mothers' milk were unrelated to postpartum depression prevalence. *Limitations*: These findings do not prove that higher omega-3 status cause lower prevalence rates of postpartum depression. Data on potentially confounding factors were not uniformly available for all countries. *Conclusions*: Both lower DHA content in mothers' milk and lower seafood consumption were associated with higher rates of postpartum depression. These results do not appear to be an artifact of cross-national differences in well-established risk factors for postpartum depression. Interventional studies are needed to determine if omega-3 fatty acids can reduce major postpartum depressive symptoms. Published by Elsevier Science B.V.

Keywords: Postpartum depression; Cross-national; Omega-3 fatty acids; Docosahexaenoic acid; Arachidonic acid; Nutrition; Seafood; Meta-analysis; Ecological; Epidemiology

1. Introduction

Mothers are the sole source of nutrients for the fetus during development. Without adequate nutri-

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tional replenishment, mothers can become depleted of critical nutrients during pregnancy with adverse consequences for both mother and infant. Hibbeln and Salem Jr. (1995) previously proposed that mothers may be at a higher risk of suffering postpartum depression when they become depleted of omega-3 essential fatty acids, in particular docosahexaenoic acid (DHA). Maternal DHA status can be reduced by half during pregnancy and not fully restored at 26 weeks postpartum (Holman et al., 1991; Al et al., 1995; Otto et al., 1997). DHA is selectively transferred from the maternal circulation to the fetus by a placental protein (Cambell et al., 1998). An adequate supply of maternal DHA is necessary to support optimal neurological development of both fetus and infant (Salem Jr., 1989; Willatts et al., 1998; Birch et al., 2000). DHA is highly concentrated in synaptic neuronal membranes and has unique membrane biophysical properties critical to synaptic function (Salem Jr., 1989). Synaptic growth cones, the progenitors of synapses and dendrites, preferentially accumulate DHA during neuronal development (Auestad and Innis, 2000; Martin, 1998). Synaptic growth cones become depleted of DHA when rat mothers consume diets restricted in omega-3 fat content (Auestad and Innis, 2000). Shortening of dendrites and less dendritic branching occurred in rat pups whose mothers were fed diets deficient in essential fatty acids (Wainwright et al., 1998). When supplied in infant formula at adequate doses, DHA and arachidonic acid (AA) improve infant cognitive development and visual acuity (Willatts et al., 1998; Birch et al., 2000; Clandinin et al., 1997). DHA and AA cannot be synthesized de novo by either the mother or the fetus. Production of DHA and AA from essential precursors is inadequate to support the developmental needs of infants; thus preformed sources are required (Salem Jr. et al., 1996). Fish and seafood are prominent dietary sources of preformed omega-3 fatty acids DHA and eicosapentaenoic acid (EPA).

DHA and or EPA depletion due to pregnancy may have adverse neuropsychiatric consequences for mothers. A growing body of data supports the proposition (Hibbeln and Salem Jr., 1995) that an inadequate intake of omega-3 fats is associated with major depression and other affective disorders. Several investigators have reported lower plasma and erythrocyte concentrations of omega-3 fats among depressed subjects (Adams et al., 1996; Peet et al., 1998; Edwards et al., 1998; Maes et al., 1996). In a recent placebo-controlled clinical trial, the treatment response to EPA plus DHA among subjects with bipolar affective disorder was robust enough that the trial could be stopped after 4 months (Stoll et al., 1999). The treatment group had significantly fewer depressive episodes. A significant antidepressant effect of 1 g/day of EPA alone among subjects with treatment resistant depression has also recently been described (Peet et al., personal communication). However, since EPA is also converted in to DHA in vivo (Salem Jr. et al., 1996), it is difficult to definitively determine the relative effects of each fatty acid. One recent study reported that seafood consumption greater than twice/week is associated with a lower risk of both depression (odds ratio = 0.63) and suicidal ideation (odds ratio = 0.57) (Tanskanen et al., 2001). Consistent with these findings, a prior cross-national analysis reported that greater seafood consumption was strikingly correlated with a lower lifetime prevalence rates of major depression ($r = -0.84$, $p < 0.005$) (Hibbeln, 1998). Since greater seafood consumption protects women from depletion of DHA and EPA during pregnancy (Al et al., 1995; Makrides et al., 1996), the central hypothesis of this study was that the prevalence rates of postpartum depression should be lower in countries with greater rates of seafood consumption. The DHA content of mothers' breast milk is a biological marker for maternal omega-3 fatty acid status in the postpartum (Al et al., 1995; Makrides et al., 1996). Thus, a secondary hypothesis was that higher concentrations of DHA in mothers' milk would predict lower rates of postpartum depression across countries.

In this cross-national ecological study, several strategies were employed to evaluate and reduce the influence of confounding factors. Only published studies using the Edinburgh Postpartum Depression Scale (EPDS) were included to ensure greater uniformity and comparability of the category of major postpartum depressive symptoms. The EPSD was specifically designed to evaluate the prevalence and severity of postpartum depression (Cox, 1994). In contrast to other depression rating scales, the EPDS excludes biological symptoms that are common to

both depression and normal postpartum states, e.g., sleep difficulties (Cox, 1994). The EPDS has been translated into more than 17 languages and has demonstrated excellent selectivity and in multiple validation studies (O'Hara, 1994, Boyce et al., 1993, Jadresic et al., 1995; Abou-Saleh and Ghubash, 1997, Carpiniello et al., 1997; Fossey et al., 1997; Da-Silva et al., 1998; Lawrie et al., 1998; Lee et al., 1998). Since validation studies were not conducted in all countries included in this study, differences in diagnostic yield may have existed. However, a conservative interpretation is that a score above a high cut-off (e.g., 12/13) indicated severe depressive symptoms, rather than a major depression. Adverse personal, social and economic conditions clearly increase the risk of suffering severe depression symptoms in the postpartum period (O'Hara and Swain, 1996). Thus, the impact of the following factors were evaluated using the available published data: study time postpartum, low socioeconomic class, the percentage of young mothers, the percentage of mothers without partners, the percentage of mothers with secondary education and the influence of Asian cultures.

2. Methods

Literature searches were conducted using Internet Grateful Med and Pubnet Med (National Library of Medicine, Bethesda, MD, USA) using applicable search terms including: postpartum depression, postnatal depression, Edinburgh Postnatal Depression Scale, cross-cultural depression, breast milk, mothers' milk, fatty acids, omega-3 fats and essential fats. The fatty acid compositions of mothers' milk were reported as area percent or calculated as weight percent. DHA, EPA and AA values were averaged across studies in countries with multiple reports. Data describing apparent seafood consumption came from a single source document published by the National Marine Fisheries Service and the Food and Agriculture Organization of the United Nations (World Health Organization, 1996). Apparent seafood consumption is an economic measure of disappearance of seafood from the economy (catch plus imports minus exports). Seafood consumption for South Africa and the United Arab Emirates was estimated by averaging values from bordering countries.

Prevalence studies were included if they (1) reported the prevalence rates of major postpartum depressive symptoms, (2) used the EPDS instrument to assess postpartum depression, (3) were published as primary data and (4) reported appropriate methodology regarding sampling and data analysis. All studies assessed point prevalence among consecutive admissions to give birth except for the South Australia Health Omnibus Survey, which was a large study that utilized population sampling techniques (Wilson et al., 1992). One study was excluded because it sampled depression among mothers of sick infants (Barnett et al., 1993) and a second (Guo, 1993) because it utilized a poorly described mail-in survey. The inclusion or exclusion of any of these three studies did not significantly alter the results. In most cases the cut-off of 12/13 was used to identify major postpartum depressive symptoms as established by Cox (1994). In some studies (Carpiniello et al., 1997), comparisons to the sensitivity and specificity to other depression scales in comparison of major vs. minor depressive symptoms mandated the use of an alternative cutoff (Table 1). Since the occurrence and severity of postpartum depression varies over time (Cox, 1994) the study time was selected as 3 months, reporting depressive symptoms over the last 7 days, whenever possible (Table 1).

Multiple reports on the point prevalence of postpartum depression were available in five countries, Australia (MacLennan et al., 1996; Stamp and Crowther, 1994; Boyce et al., 1993; Griepsma et al., 1994; Brown and Lumley, 1998; Condon and Corkindale, 1997), New Zealand (McGill et al., 1995; Holt, 1995; Webster et al., 1994), Sweden (Lundh and Gyllang, 1993; Wickberg and Hwang, 1996; Bagedahl-Strindlund and Monsen Borjesson, 1998), the United Kingdom (Cox et al., 1987, 1993; Warner et al., 1996; Appleby and Whitton, 1993; Cooper et al., 1996; Thompson et al., 1998; Hearn et al., 1998) and the United States (Stuart et al., 1998; Roy et al., 1993; Reighard and Evans, 1995; Schaper et al., 1994). Data were combined in a meta-analysis using the method described by O'Hara and Swain (1996) to represent the mean prevalence rate for each country. This mean prevalence was determined by dividing the number of all women with major

Table 1
Prevalence rates, seafood consumption and population characteristics

Country		Seafood consumption (lb/person/year)	PPD (%)	Study *n*	Days postpartum	EPSD cut-off	Age (years)	% Low SES	% No partner	% Sec. education
Singapore	Kok et al., 1994	81.1	0.5	200	90	12/13	ND	ND	ND	ND
Japan	Tamaki et al., 1997	147.7	2.0	267	30	12/13	ND	ND	ND	ND
Iceland	O'Hara, 1994	225.0	2.5	200	ND	12/13	ND	ND	ND	ND
Malaysia	Kit et al., 1997	60.0	3.0	154	45	12/13	28.7	ND	ND	52.3
Chile	Jadresic et al., 1995	65.7	5.5	108	75	12/13	27.7	0.0	10.0	99.0
Hong Kong	Lee et al., 1998	127.6	5.5	145	45	9/10	29.0	1.0	0.0	46.0
Sweden	Mean*	59.1	8.3	1584	90	11/12	28.0	ND	8.0	ND
Switzerland	Righetti-Veltema et al., 1998	29.5	10.2	570	90	12/13	30.1	22.3	5.0	42.0
France	Fossey et al., 1997	63.9	11.0	126	240	12/13	ND	ND	ND	ND
Ireland	Lane et al., 1997	33.3	11.0	370	45	12/13	28.9	56.0	13.0	86.0
United States	Mean*	48.1	11.5	1612		12/13	28.1	15.3	ND	ND
Israel	Fisch et al., 1997	46.1	12.4	327	75	9/10	28.9	9.9	0.3	50.0
Canada	Bernazzani et al., 1997	50.7	12.7	213	180	12/13	29.3	9.9	0.0	78.3
Spain	Sebastian Romero et al., 1999	83.8	13.6	190	ND	ND	30.1	ND	25.0	56.0
Netherlands	Pop et al., 1992	25.1	14.0	293	74	ND	29.1	11.0	0.0	ND
UK	Mean*	40.8	14.4	9128		12/13	ND	ND	ND	ND
Italy	Carpiniello et al., 1997	48.7	15.0	61	75	9/10	31.6	ND	ND	ND
New Zealand	Mean*	39.0	17.4	1657	30	12/13	24.2	ND	12.7	ND
United Arab Emirates	Abou-Saleh and Ghubash, 1997	13.1	18.0	ND	52	12/13	ND	ND	ND	ND
Australia	Mean *	41.2	18.6	5057		12/13	ND	ND	ND	ND
W. Germany	Bergant et al., 1998	27.6	20.0	110	4	10/11	ND	ND	ND	ND
Brazil	Da-Silva et al., 1998	12.6	24.1	33	30	13/14	21.5	100.0	38.0	0.0
South Africa	Lawrie et al., 1998	8.6	24.5	108	90	11/12	28.1	95.0	30.4	19.6

*Indicates mean derived from meta-analysis. See Table 2. 'Study *n*' indicates number of study subjects. 'Days postpartum' indicates the study time postpartum. 'EPSD cut-off' is the rating used in each study to define major postpartum depression. '% low SES' indicates the percentage of the study population with the lowest socioeconomic scale rank. '% no partner' indicates the percentage of women unmarried or without support of the father. '% sec. education' indicates the percentage of women completing 12th grade or equivalent. ND indicates data not available.

postpartum depressive symptoms by the total number of women across all studies and multiplied by 100 to calculate percent.

3. Statistical methods

In the primary analyses, a simple Pearson's product moment correlation and a Spearman's rank coefficient test compared the content of DHA, EPA and AA in mothers' milk to the prevalence rates of postpartum depression across countries. Residuals were examined and curve fitting was performed. In the secondary analyses, potential confounding risk factors that are known to predict postpartum depression were evaluated. Multivariate analyses that simultaneously included all potential confounding factors were not possible, as data on every factor were not available for each study and the missing data would have severely distorted the results. Thus secondary analyses were conducted in order to evaluate the impact of each risk factor (e.g., percentage of the sample with low socioeconomic status) on the cross-national prevalence rates of postpartum depression. These secondary analyses were a series of simple univariate regressions that compared each potentially confounding factor to prevalence rates of major postpartum depressive symptoms. Thus, these secondary analyses identified countries in which the sample population had extreme outliers in these factors. A tertiary series of simple univariate analyses and logarithmic regression analyses were then performed using models that excluded countries with extreme outliers (e.g., 100% of the population having low socioeconomic status). Asian countries were also considered as potential outliers a priori due to cultural differences. Finally, to assess the robustness, the results of the primary analyses, which contained all countries, were compared to the tertiary analyses that had sequentially that excluded countries with extreme outliers in potentially confounding factors.

4. Results

The total sample size of this analysis included 14 532 subjects over 23 countries described in 41 studies. Only three studies contained less than 100 subjects and inclusion or exclusion of the studies did not significantly alter the results. Twenty-two different countries were identified that met study criteria and reported of point prevalence rates of major postpartum depressive symptoms (Tables 1 and 2). Data on the prevalence of postpartum depression in Iceland were reported as a secondary source (O'Hara, 1994) and did not meet inclusionary criteria. Because this population had unique characteristics of seafood consumption and latitude, these data were evaluated in secondary analyses. Published data on the DHA, EPA and AA compositions of mothers' milk were found for 16, 12 and 15 countries, respectively (Table 3). Data from Eskimos was included to describe the maximum human physiological range of DHA composition in milk, although no postpartum depression data was available (Innis and Kuhnlein, 1988).

4.1. Results: primary analysis

The prevalence of postpartum depression varied nearly 50-fold from a low of 0.5% in Singapore to a high of 24.5% in South Africa (Kok et al., 1994; Lawrie et al., 1998). The mean prevalence rate world-wide was 12.4% (6.5 S.D., $n = 22$ countries). Higher national seafood consumption predicted a lower prevalence rates of postpartum depression ($r = -0.75$, $F = 25.8$, $p < 0.0001$, $n = 22$) in a simple regression model. An examination of the residual plots of these findings suggested that a non-linear curve might better describe the relationship of the higher seafood consumption to the prevalence of postpartum depression. A logarithmic equation [$y = 40.90 - 7.60\ln(x)$] was a better fit for describing this relationship ($r = -0.81$, $p < 0.0001$) (Fig. 1). Higher DHA content in mothers' milk also predicted a lower prevalence rates of postpartum depression, ($r = -0.84$, $F = 34.0$, $p < 0.0001$, $n = 16$) (Fig. 2). Greater apparent seafood consumption predicted DHA content of mothers' milk ($r = 0.66$, $F = 10.7$, $p < 0.006$, $n = 16$). This result was consistent with reports of the influence of dietary intake of EPA and DHA on the composition of DHA in breast milk (Harris et al., 1984; Van Houwelingen et al., 1995; Makrides et al., 1996). The results from Spearman rank analyses were similar to these Pearsons product

Table 2
Descriptive data used for meta-analysis; prevalence rates, seafood consumption and population characteristics

Country		PPD (%)	Total *n*	Depressed *n*	Days postpartum	EPSD cut-off	Age (years)	% Low SES	% No partner
Australia	Griepsma et al., 1994	57.8	185	107	56	12/13	ND	12	ND
Australia	Brown and Lumley, 1998	16.9	1331	225	180	12/13	ND	ND	ND
Australia[33]	Condon and Corkindale, 1997	12	212	25	30	12/13	ND	23	ND
Australia[30]	Boyce et al., 1993	8.7	103	9	180	12/13	2.4	ND	6
Australia[29]	Stamp and Crowther, 1994	9.0	222	21	45	12/13	28	4	14
Australia[28]	MacLennan et al., 1996	18.5	3004	556	30	ND	ND	ND	ND
Australia	Mean*	18.6	5057	943					
New Zealand	McGill et al., 1995	20	1330	262	180	12/13	ND	ND	ND
New Zealand	Webster et al., 1994	7.8	206	16	30	12/13	27.5	ND	12.7
New Zealand	Holt, 1995	9.0	121	11	45	12/13	ND	ND	ND
New Zealand	Mean*	17.4	1657	289					
Sweden	Wickberg and Hwang, 1996	8.3	1584	131	90	11/12	28	ND	8
Sweden	Lundh and Gyllang, 1993	7.0	258	18	90	12/13	ND	ND	ND
Sweden	Bagedahl-Strindlund and Monsen Borjesson, 1998	14.5	309	45	90	12/13	28	ND	6.4
Sweden	Mean*	9	2151	194					
United Kingdom	Warner et al., 1996	11.8	2375	280	58	12/13	28	ND	14.8
United Kingdom	Cox et al., 1987	25	84	21	90	12/13	26	7	6
United Kingdom	Cooper et al., 1996	15.3	5124	784	45	12/13	ND	ND	ND
United Kingdom	Cox et al., 1993	13.6	464	63	180	12/13	26.3	1.5	9.2
United Kingdom	Appleby and Whitton, 1993	12	158	19	45	12/13	ND	ND	ND
United Kingdom	Thompson et al., 1998	16.1	747	120	90	12/13	ND	ND	ND
United Kingdom	Hearn et al., 1998	17	176	30	42	11/12	ND	ND	ND
United Kingdom	Mean*	14.4	9128	1317					
United States	Schapner et al., 1994	8.0	1139	92	45	12/13	28.1	15.3	ND
United States	Stuart et al., 1998	23.3	107	25	98	12/13	ND	ND	0
United States	Roy et al., 1993	17.4	185	32	45	12/13	ND	ND	ND
United States	Reighard and Evans, 1995	19.9	181	36	ND	12/13	ND	ND	ND
United States	Mean*	11.5	1612	185					

*Mean was derived by the sum of the number of depressed subjects divided by the sum of the number of subjects studied across all studies for that country. ‘PPD %’ indicates percentage with severe postpartum depression. ‘Study *n*’ indicates number of study subjects. ‘Days postpartum’ indicates the study time postpartum. ‘EPSD cut-off’ is the rating used in each study to define major depressive symptoms. ‘% low SES’ indicates the percentage of the study population with the lowest socioeconomic scale rank. ‘% no partner’ indicates the percentage of women unmarried or without support of the father. ND indicates data not available.

Table 3
AA, EPA and DHA content of mothers' milk

Country	AA wt.%	EPA wt.%	DHA wt.%	Country	AA wt.%	EPA wt.%	DHA wt.%
South Africa average	**0.80**	**0.12**	**0.15**	**Sweden average**	**0.44**	**0.09**	**0.34**
van der Westhuizen et al., 1988	1.00	0.1	0.10	Yu et al., 1998	0.46	0.09	0.29
van der Westhuizen et al., 1988	0.60	0.1	0.20	Jansson et al., 1981	0.40	ND	0.30
Italy; Serra et al., 1997	**0.47**	**0.17**	**0.12**	Horby-Jorgensen et al., 1996	0.47	ND	0.43
USA average	**0.54**	**0.07**	**0.17**	**Spain average**	**0.63**	**0.15**	**0.34**
Finley et al., 1985	0.29	ND	0.06	Villacampa et al., 1982	0.57	0.15	0.30
Harris et al., 1984	0.40	ND	0.10	de Lucchi et al., 1988	0.80	ND	0.40
Putnam et al., 1982	0.60	0.1	0.10	Rueda et al., 1998	0.66	ND	0.33
Spear et al., 1992	0.58	0.04	0.15	**France average**	**0.45**	**0.03**	**0.35**
Dotson et al., 1992	0.53	0.07	0.16	Maurage et al., 1998	0.49	0.03	0.47
Jackson et al., 1994	0.56	0.06	0.16	Martin et al., 1993	0.36	ND	0.24
Carlson et al., 1986	0.59	ND	0.19	Chardigny et al., 1995	0.50	0.02	0.32
Francois et al., 1986	0.50	0.1	0.20	Guesnet et al., 1993	0.45	ND	0.37
Bitman et al., 1983	0.60	ND	0.23	**Canada average**	**0.57**	**0.17**	**0.35**
Henderson et al., 1998	0.52	ND	0.21	Innis et al., 1994	0.50	0.2	0.20
Specker et al., 1987	0.69	ND	0.27	Clandinin et al., 1997	0.54	0.13	0.30
Australia average	**0.40**	**0.1**	**0.25**	Cherian and Sim, 1996	0.40	ND	0.30
Makrides et al., 1995	0.40	0.07	0.21	Clandinin et al., 1981	0.50	0.12	0.40
Makrides et al., 1996	0.41	0.08	0.21	Innis and Kuhnlein, 1988	0.70	0.2	0.40
Gibson and Kneebone, 1981	0.40	0.16	0.32	Innis et al., 1990	0.80	0.2	0.50
UK average	**0.27**	**ND**	**0.25**	**Israel**	**0.58**	**ND**	**0.37**
Hall, 1979	0.07	ND	0.08	Budowski et al., 1994			
Sanders and Reddy, 1992	0.38	ND	0.30	**Hong Kong**	**0.61**	**0.05**	**0.56**
Sanders and Reddy, 1992	0.35	ND	0.37	Chen et al., 1997			
Germany average	**0.49**	**0.05**	**0.29**	**Chile** Valenzuela and Uauy, 1999	ND	**ND**	**0.74**
Harzer et al., 1983	0.39	0.05	0.16	**Japan average**	**0.68**	0.15	**0.81**
Koletzko et al., 1988	0.36	0.04	0.22	Ogunleye et al., 1991	0.36	0.2	0.53
Genzel-Boroviczeny et al., 1997	0.45	0.05	0.23	Wang et al., 2000	0.99	0.1	1.09
Fidler et al., 1998	0.77	0.07	0.55	**Malaysia average**	**0.56**	**ND**	**0.84**
Netherlands average	**0.46**	**0.07**	**0.30**	Kneebone et al., 1985	0.64	ND	0.71
Beijers and Schaafsma, 1996	0.31	0.07	0.24	Kneebone et al., 1985	0.47	ND	0.90
Foreman-van Drongelen et al., 1996	0.52	0.04	0.26	Kneebone et al., 1985	0.57	ND	0.90
Carnielli et al., 1998	0.48	0.07	0.26	**Eskimo (for comparison)**	**0.60**	**1.1**	**1.40**
Beijers and Schaafsma, 1996	0.37	0.07	0.34	Innis and Kuhnlein, 1988			
Jacobs et al., 1996	0.60	0.1	0.40				

Average data for each country are expressed using bold, underlined values. AA wt.%, EPA wt.% and DHA wt.% indicate the weight percentage of total fats in mature mothers' milk. ND indicates data not available.

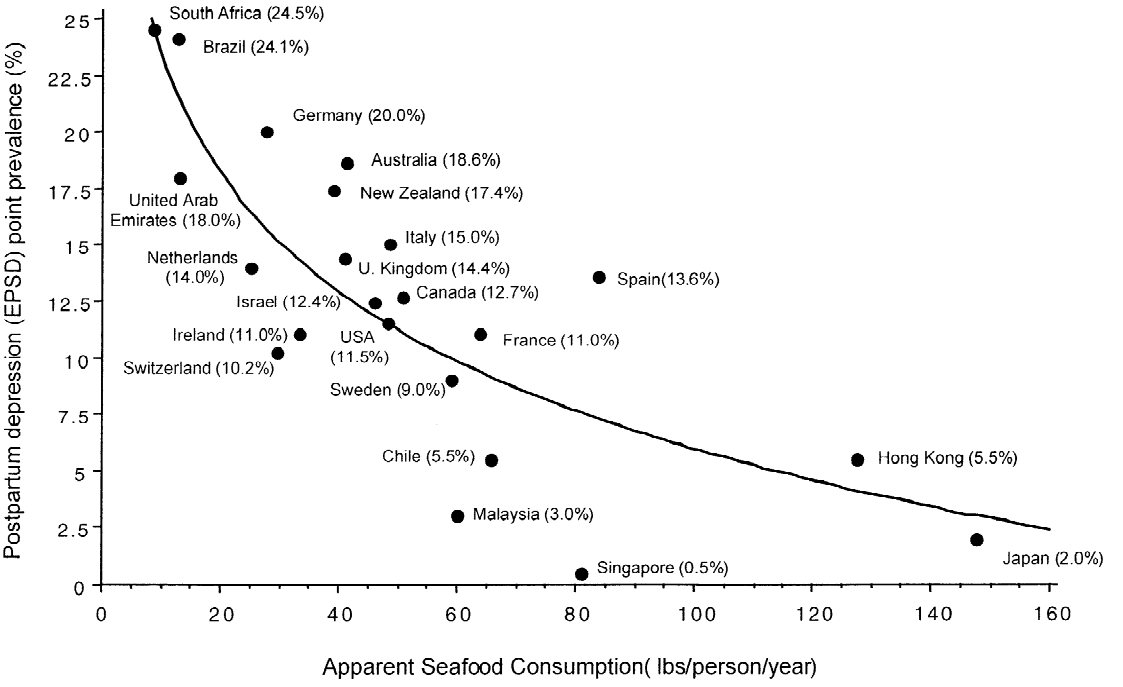

Fig. 1. Seafood consumption and prevalence rates of postpartum depression. Postpartum prevalence rates for Australia, New Zealand, Sweden and the United Kingdom, The United States were derived by meta-analysis. All other countries are represented by a single study, see text. Apparent Seafood consumption lb/person/year is an economic measure of disappearance of all fish and seafood from the economy and is calculated by imports plus catch minus exports. A logarithmic regression was used for analysis ($r = -0.81$, $p < 0.001$).

moment correlations. A logarithmic model did not create a better fit for the relationship between the DHA content of breast milk and the prevalence of postpartum depression in comparison to the simple regression models. In simple and logistic regression models, the AA ($n = 15$) and EPA ($n = 12$) content of mothers' milk were unrelated to either the prevalence rates of postpartum depression or to rates of apparent seafood consumption.

4.2. Secondary analysis: examination for potentially confounding factors

An assessment of the impact of population differences in well-established risk factors on the point prevalence rates of postpartum depression was conducted with series of secondary analyses. This series of simple regression models evaluated the following potentially confounding factors: age, the percentage of subjects with low socioeconomic status, the percentage of women without partners, the percentage of the sample completing secondary education, the sample time postpartum and geographical latitude. Unfortunately, data on each of these parameters were not reported in most publications. The following factors did not predict prevalence rates of postpartum depression: the postnatal study time ($r = 0.02$, $p < 0.93$, $n = 38$ studies), the percent of women unemployed or housewives ($r = 0.07$, $p < 0.86$, $n = 8$ studies), the percent of unmarried women ($r = 0.06$, $p < 0.86$, $n = 12$ studies) and the latitude $r = -0.14$, $p < 0.52$, $n = 23$ countries).

In this study, the risk factors that predicted the prevalence rates of postpartum depression in simple correlations included; (1) low socioeconomic status, (2) young maternal age, (3) the percentage of women without partners, (4) percentage with a secondary education. One or two countries with extreme values drove these relationships for each risk factor. The correlational relationship between low socioeconomic status and the prevalence of postpartum depression ($r = 0.88$, $p < 0.004$, $n = 9$

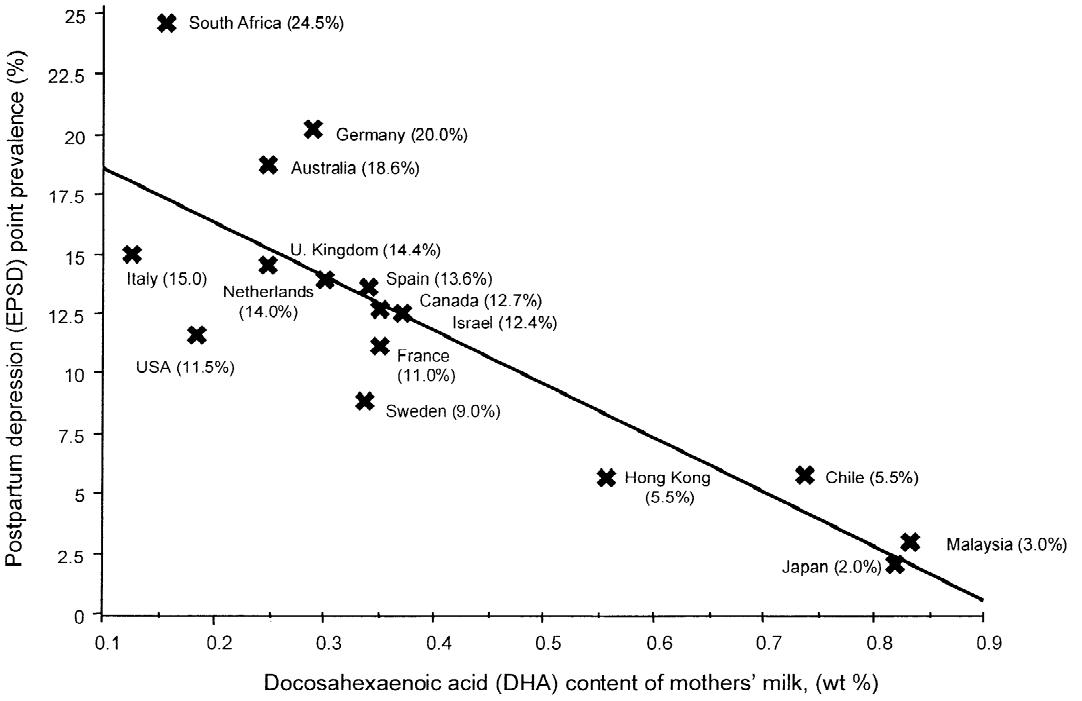

Fig. 2. DHA contents of mothers' milk and prevalence rates of postpartum depression. Postpartum prevalence rates for Australia, Sweden, the United Kingdom, The United States were derived by meta-analysis. All other countries are represented by a single study, see text. DHA content of mother's milk is expressed as the weight percent of docosahexaenoic acid of mature milk. A simple Pearson's product moment correlation was used for regression analysis ($r = -0.84$, $p < 0.0001$).

countries) was substantially influenced by Brazil and South Africa. The sample populations of these countries had rates of 100% and 95% low socio-economic status, respectively, compared to the mean percentage of the entire sample prevalence rate of 24.5% (S.D. 25.6%). The correlational relationship between the percent of women without a partner and the prevalence rates of postpartum depression ($r = 0.76$, $p < 0.02$, $n = 10$) was also substantially influenced by Brazil (38%) and South Africa (34.4%). These countries appeared to be outliers as the mean percent of women without a partner for the entire sample was 10.4% (S.D. 10.6%). The correlational relationship between the percent of women with a secondary education and the prevalence rates of postpartum depression ($r = 0.67$, $p < 0.03$, $n = 10$) was also substantially influenced by Brazil (0%) and South Africa (20%). These countries appeared to be extreme values as the mean percent of women with a secondary education for the entire sample was 52.9% (S.D. 29.7%). The correlational relationship between age and the prevalence rates of postpartum depression ($r = -0.44$, $p < 0.05$, $n = 21$) was heavily influenced by Brazil (21.4 years). In contrast the mean age of mothers in the full sample was 28.4 years (S.D. 1.3). Thus, Brazil and South Africa were identified as countries that could potentially confound the findings reported in the primary analyses.

4.3. Results: assessment of robustness of the primary analysis

A tertiary series of simple correlational models was performed that excluded each of the countries that had extreme values for the potentially confounding risk factors. In addition, a model was constructed that excluded all Asian countries. The results of this tertiary series of regression models were not substantially different from the primary models that included all 22 countries. The results of the tertiary regression

models that excluded Brazil and controlled for outliers of age were: $r = -0.73$, $p < 0.0002$ (simple); $r = -0.78$, $p < 0.0001$, $n = 21$ (logarithmic). The results of the models that excluded Brazil and South Africa and controlled for outliers of low socioeconomic status and the percentage of women without partners were; $r = -0.73$, $p < 0.002$ (simple) and $r = -0.71$, $p < 0.0001$, $n = 20$ (logarithmic). Exclusion of all Asian countries also produced similar results; $r = -0.69$, $p < 0.002$, (simple) $r = -0.76$, $p < 0.0001$, $n = 18$ (logarithmic). Inclusion of Iceland did not fundamentally alter the results; $r = -0.71$, $p < 0.0001$ (simple); $r = -0.83$, $p < 0.0001$, $n = 23$ (logarithmic). The relationship between higher DHA content of mothers' milk and lower prevalence rates of postpartum depression ($r = -0.84$, $p < 0.0001$, $n = 16$) was also not significantly altered by the exclusion of Brazil and South Africa ($r = -0.86$, $p < 0.0002$, $n = 15$), nor by the exclusion of all Asian countries ($r = -0.68$, $p < 0.001$, $n = 13$), in simple regression models. In conclusion, these regression models described substantial associations between lower prevalence rates of postpartum depression and both higher rates of seafood consumption and the higher content of DHA in mothers' milk. These findings were robust despite corrections for age, low socioeconomic status, percentages of women without partners, percentages of women with secondary education and countries of Asian origin.

5. Discussion

The findings in these cross-national analyses were clearly consistent with the hypothesis (Hibbeln and Salem Jr., 1995) that inadequate dietary intake of omega-3 fats and the subsequent maternal depletion of omega-3 fats during pregnancy are associated with an increased risk of major postpartum depressive symptoms. Both lower concentrations of DHA in mothers' milk and lower national rates of seafood consumption were robustly correlated with higher rates of major postpartum depressive symptoms in several models of analysis. These data suggest that the nearly 50-fold difference in prevalence rates of major postpartum depressive symptoms across countries is substantially associated with omega-3 fatty acid nutritional status. The concentrations of DHA in mother's milk are a reasonably good measure of maternal DHA status in the postpartum period (Otto et al., 1997; Van Houwelingen et al., 1995). However, we note that since DHA is selectively concentrated in breast milk in comparison to EPA (Francois et al., 1986), thus DHA in breast milk may be a surrogate marker for an insufficiency in other omega-3 fatty acids which may be important in affective disorders. The finding that the AA content of breast milk was unrelated to the prevalence of postpartum depression suggests a specific relationship to omega-3 fatty acid status.

One possible criticism of these cross-national findings is that women from Asian cultures may have been more reluctant to express symptoms of psychiatric illnesses, which resulted in artificially low reports of prevalence rates. In addressing this criticism, it should first be noted that despite exclusion of all Asian countries from these analyses, the cross-national relationships remained robust. In addition, studies that directly compared postpartum depression among Asian and non-Asian populations do not support this criticism (Matthey et al., 1997; Shimizu and Kaplan, 1987; Yoshida et al., 1997). Low rates of severe postpartum depressive symptoms in Japan have been reported with good consistency. Although a study of 627 Japanese women reported a rate of 18.2% for maternity blues and minor depression (Tamaki et al., 1997), the rate of severe depressive symptoms, at a cutoff of 12/13, was 3.5% at 3 months (Okano, personal communication). In an earlier study of 122 women from the same city reported a rate of major postpartum depressive symptoms of 2.0% (Okana, 1989). Okano et al. (Okano et al., 1998) examined the hospital records of 93 739 live births, and reported a rate of only 0.34/1000 subsequent psychiatric admissions in the 3 months postpartum. Thus, the existing literature does not support the proposition that differences in cultural factors or social support can account for the lower rates of postpartum depression among Japanese women compared to American women.

Careful consideration was given to the issue of potentially confounding factors. Thus the risk factors for postpartum depression that have been well established in the literature were identified and data from the sample populations were evaluated, when avail-

able. Consistent with other reports, the power of these risk factors is comparatively small. For example, the largest meta-analysis risk factors for postpartum depression (O'Hara and Swain, 1996) identified recent life events ($r = 0.29$) social support ($r = 0.30$) as the most powerful factors. Socioeconomic factors: family income and mother's occupation (mean correlations of 0.07 and 0.073, respectively) were significant but very weak predictors. Thus, even though the data on these risk factors is not complete for all the countries, the influence of the total known confounding variables would be of low power compared to the predictive value of breast milk composition of DHA or rates of seafood consumption. Thus, the relationships between both seafood consumption and the DHA content of mothers' milk do not appear to be artifacts of cross-national differences in well-established risk factors for postpartum depression.

Despite the use of a uniform symptom scale, this study has several limitations. First, the seafood consumption and breast milk concentration data presented here can only be assumed to reflect relative differences comparing countries. However, the seafood consumption data did come from a single source document and quantifies rates of consumption for each nation as a whole, and thus provides reasonable data to compare countries. Unfortunately, measures of the fatty acid content obtained directly from the plasma or breast milk from each woman in each study were not available. Likewise, the prevalence rates of postpartum depression across countries were comparative estimates based on available data and may reflect true prevalence rates in only a limited manner. A high score on the EPSD indicates severe depressive symptoms in the postpartum, which may be part of the symptom complex of numerous psychiatric disorders, including major depression. Thus, these findings may not be specific to postpartum depression, but may indicate a general relationship between omega-3 status and risk of depressive symptoms in other psychiatric disorders. None the less, the correlational relationships described here between both DHA in mother's milk and seafood consumption and prevalence of postpartum depression are nearly identical with regards to the order of magnitude and direction compared to a prior cross-national analysis examining prevalence rates of major depression (Hibbeln, 1998). These findings are also similar to the cross-national relationships between seafood consumption and lifetime prevalence rates of bipolar spectrum disorder ($r = -0.85$, $p < 0.004$) and bipolar II disorder ($r = -0.89$, $p < 0.004$) (unpublished data).

The results of this cross-national analysis do not prove that there is a causal relationship between improving maternal omega-3 fatty acid status and a reduction in the risk or severity of postpartum depression. However, this causal relationship can be readily and safely tested. Supplementation with omega-3 fatty acids from both marine and algal sources during pregnancy is not only safe but has several important benefits during pregnancy including longer gestational times and greater birth weights (Harris et al., 1984; Makrides et al., 1996; Olsen, 1993; Olsen et al., 2000). Supplementation with 2.7 g/day of EPA plus DHA during the last trimester increased mean birth-weight and gestation time up to an average of 7 days among infants whose mothers had a poor baseline omega-3 status (Olsen et al., 1992). In a multi-center trial of 898 women at 19 centers, reported a decreased risk of preterm delivery, but found no significant adverse side effects after supplementation with doses ranging from 2.7 g/day to 6.1 g/day of EPA plus DHA (Olsen et al., 2000). No adverse side effects, specifically no increased bleeding times or hemorrhage during parturition, were observed in a treatment study of 223 women with high-risk pregnancies including gestational diabetes and pre-eclampsia (Onwude et al., 1995). Supplementation with 1.1 g DHA/day increased breast milk concentrations to 0.8% (Harris et al., 1984; Makrides et al., 1996) without adverse effects. This milk concentration is similar those reported in Asian countries such as Malaysia (Kneebone et al., 1985) where low rates of postpartum depression were reported. A current recommendation is that pregnant women should consume a minimum of 650 mg/day of EPA plus DHA with a minimum of 300 mg/day as DHA (Simopoulos et al., 1999). Given the balance of significant potential benefits with low potential risks, controlled intervention trials should be conducted to determine if omega-3 fatty acids could prevent major depressive symptoms in the postpartum or if they might provide a viable alternative to pharmacological treatments.

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