Public Health Nutrition: 12(12), 2343–2351 doi:10.1017/S1368980009004935

Plasma *n*-3 fatty acids and psychological distress in aboriginal Cree Indians (Canada)

Michel Lucas[1], Éric Dewailly[1,2,*†], Carole Blanchet[1], Suzanne Gingras[1] and Bruce J Holub[3]

[1]Public Health Research Unit, Laval University Medical Research Centre (CHUQ), Sainte-Foy, Québec, Canada: [2]Department of Social and Preventive Medicine, Laval University, Sainte-Foy, Québec, Canada: [3]Department of Human Biology and Nutritional Sciences, University of Guelph, Guelph, Ontario, Canada

Submitted 19 June 2008: Accepted 11 December 2008: First published online 26 February 2009

Abstract

Objective: To examine the relationship between psychological distress (PD) and plasma *n*-3 long-chain (LC) PUFA, i.e. EPA, docosapentaenoic acid (DPA*n*-3) and DHA.

Design: Population-based, cross-sectional Santé-Québec Health Survey (1991). Participants were categorized as high-level PD if they scored over the 80th percentile of the PD Index in the Santé-Québec Survey; non-distressed subjects were those who scored less than this cut-off. Associations between tertiles of *n*-3 fatty acids (FA) and the risk of high-level PD were expressed as odds ratios, with the lowest tertile as the reference group.

Setting: Québec, Canada.

Subjects: Data were analysed from a representative sample of 852 James Bay Cree Indian adults aged 18 years and over.

Results: Proportions of *n*-3 FA were statistically significantly lower in the PD than in the non-distressed group. After adjustment for confounders, EPA was the only individual *n*-3 FA significantly associated with the risk of high-level PD. Combinations of EPA + DHA or EPA + DPA*n*-3 + DHA or the sum of *n*-3 were also associated with the risk of high-level PD. Compared with the lowest tertile of EPA + DHA, the OR for high-level PD was 0·89 (95 % CI 0·59, 1·36) for the second and 0·56 (95 % CI 0·32, 0·98) for the third tertile, after controlling for confounders.

Conclusions: In the present retrospective, cross-sectional study, we found that proportions of *n*-3 LC PUFA in plasma phospholipids, markers of *n*-3 LC PUFA consumption from fish, were inversely associated with PD.

Keywords
n-3 fatty acids
Psychological distress
Cree Indians
Eicosapentaenoic acid
Docosahexaenoic acid

The shift away from traditional lifestyles and diets is associated with increasing health problems in several native populations[1,2]. Some aboriginal groups have reported evidence of severe psychological distress (PD), with high rates of depression, suicide, violence, alcoholism and substance abuse, the most profound impact being felt by the young[1,3–7]. However, the psychiatric literature on the Cree is scarce. In a study of mental health service use between 1986 and 1988, depression was the most common psychiatric illness noted among 242 Cree receiving help from nursing and medical personnel[8]. Their traditional eating habits have been changed by cultural and environmental factors linked to modernization[9–11]. In these communities, we noted that plasma proportions of EPA + DHA were two times higher among older than among younger adults, which suggests that the former consume more traditional foods, such as fish[12].

It has been postulated that dietary changes occurring in our societies, mainly a decrease in *n*-3 (omega-3) long-chain (LC) PUFA and an increase in *n*-6 (omega-6) consumption, could be contributing to the growing incidence of depression[13]. Epidemiological and clinical studies indicate that *n*-3 LC PUFA are associated with benefits in mood disorders, particularly depression[14,15]. Although man is technically capable of endogenously synthesizing EPA and DHA from the *n*-3 precursor α-linolenic acid (α-LNA) in plants, this conversion is a very inefficient way of increasing DHA in tissues[16]. Therefore, in general, EPA and DHA measurements in blood reflect habitual dietary *n*-3 LC PUFA intake from fish[17–19].

Several biological mechanisms might potentially explain the impact on and research interest in *n*-3 fatty acids (FA) in psychiatry. Phospholipids (PL), which contain

† Correspondence address: Delta Building #2 – Office 600, 2875 Laurier Blvd, 6th Floor, Sainte-Foy (QC), Canada, G1V 2M2.

*Corresponding author: Email eric.dewailly@crchul.ulaval.ca

FA, are major components of neuronal cell membranes and are essential for normal brain functions[20]. PUFA comprise one-third of all FA in the brain[21,22]. PUFA in the brain are mainly represented by two FA, DHA and the *n*-6 arachidonic acid (AA), which constitute ≈80 % of total PUFA[21,22]. Animal experiments have indicated that *n*-3 deficiency alters serotonin neurotransmission[23–27]. In man, higher plasma DHA has been demonstrated to predict concentrations of serotonin and dopamine metabolites in cerebrospinal fluid[28,29]. Both EPA and DHA, which compete with AA for inclusion in neuronal membranes, have anti-inflammatory effects[30,31]. *n*-3 LC PUFA may also exert other influences on brain biochemistry, such as membrane structure and fluidity; enzyme, receptor, ion channel, second messenger and blood–brain barrier functions; and increase cerebral blood flow[20,32,33].

Different risk and protective factors of mental health have been identified among the James Bay Cree[34]. However, the role of their traditional diet has received scant attention with regard to mental health. A generalized measure of PD was adopted in a cross-sectional survey undertaken by the Government of Quebec among the James Bay Cree in 1991[10]. We considered it important to examine the potential role of *n*-3 LC PUFA in PD in James Bay Cree Indians.

Methods

Study design and population

The Santé-Québec Health Survey among the James Bay Cree in 1991 has been described in detail elsewhere[10,12]. Briefly, Santé-Québec, an agency of the Quebec Health and Social Services Ministry, undertook a health survey of the Cree population in 1991. The apparent long delay between the availability of these data and the results presented here is mainly due to a lack of staff and time. The primary objective of the survey was to collect relevant information on the physical, social and psychosocial health of the Cree population[10]. These data were gathered in several stages with home interviews and clinic visits. The survey targeted all private Cree households located in the nine communities of the James Bay region. Of the household respondents, 943 participants submitted to clinical measurements and blood tests. Of these, fifty did not have information on PD, twenty-six did not have FA measurements and fifteen were pregnant women; all of them were therefore excluded from the present analysis. The final sample size analysed was 852. In the survey, signed informed consent was obtained from the study subjects before inclusion. The study protocol was approved by the Clinical Research Deontology Committee of Laval University.

Psychological distress

PD among the Cree was measured via a modified version of the fourteen-Item PD Index used in the 1987 Santé-Québec Survey (PDISQS-14)[35,36]. The PDISQS-14 is an adaptation of the Psychiatric Symptom Index (PSI), developed and validated by Ilfeld[37,38]. The self-administered PDISQS-14 contains fourteen statements addressing psychological symptoms experienced in the previous week (Table 1). The structure of the PSI is based on four distinct dimensions (depression, anxiety, aggressiveness and psychomotor perturbations) connected at a second level with the more general concept of PD[39]. Scores range from a minimum of 0 to a maximum of 100. Internal consistency of the scale within Cree respondents was found to be satisfactory (Cronbach's $\alpha = 0{\cdot}94$)[34]. As in the 1987 Santé-Québec master survey[40], a high level of PD was defined by any score above the 80th percentile of the index distribution observed in the Cree. Participants were categorized as having high-level PD if they scored over the 80th percentile of the PDISQS-14 (score of 30·95). Non-distressed participants were those scoring less than this cut-off. One hundred and fifty-four participants, sixty-three men and ninety-one women, scored above the cut-off.

Table 1 The Psychological Distress Index Santé-Québec Survey (PDISQS-14) used in the Santé-Québec Health Survey among the James Bay Cree Indians

How often, during the past week, did you…
…feel hopeless about the future?
…have your mind go blank?
…feel down or blue?
…feel tense or under pressure?
…lose your temper?
…feel bored or have little interest in things?
…feel fearful or afraid?
…have trouble remembering things?
…cry easily or feel like crying?
…feel nervous or shaky inside?
…feel critical of others?
…feel easily annoyed or irritated?
…get angry over things that are not too important?
…feel like being alone?

Each item had four possible answers coded as: 0 = never, 1 = once in a while, 2 = fairly often and 3 = very often.

Plasma phospholipid fatty acids

Blood samples were collected in the fasting state. Plasma samples, stored at −80°C for ≤4 months, were measured for the FA composition of PL. FA analysis of these plasma biomarkers (PL) was based on previously published methods[41]. The results and procedures have been described in detail elsewhere[12]. Briefly, the FA composition of plasma PL was determined by capillary GLC. FA proportions in plasma PL were expressed as percentages of the total area of all FA peaks from 14 : 0 to 24 : 1. In the present study, the plasma PL proportions of FA corresponded to the relative percentages of total FA by weight. Only the proportions of PUFA are reported for the present purpose.

Statistical analysis

The statistical distribution of plasma FA was checked and found to be skewed for some FA. Therefore, we undertook

log transformation to compare FA between PD groups. Arithmetic means were also calculated for the FA data to facilitate comparisons with other studies. Student's *t* test was performed to compare FA between PD groups. ANOVA with Bonferroni correction for multiple comparisons ($P < 0{\cdot}0025$) was conducted for EPA + DHA plasma PL according to quintiles of PDISQS-14 scores. The distribution of *n*-3 FA was considered to compute cut-off points for tertiles of *n*-3. Associations between tertiles of *n*-3 FA and the risk of high-level PD were expressed as odds ratios, with the lowest tertile as the reference group. Trends across tertiles of *n*-3 FA were discerned by assigning the log-transformed median value for each tertile to all subjects in that group. Selection of co-variables was based on simulation studies[42–44], which suggested a minimum number of events per variable (minimally 10–15 events were needed per covariate). Co-variables were selected without the predictor of interest in the multivariate model and were based on backward selection, considering a liberal *P* value criterion of 0·5 for all relevant covariates[42]. The covariates tested were: age, gender, smoking status, total plasma cholesterol (<5·2 mmol/l), physical activities in leisure time, ≥1 chronic medical illness in lifetime, BMI (kg/m^2), education, occupation, marital status and no recent stress events. For the variable 'recent stress events', subjects were asked if they had experienced any of six stressful events during the past 12 months: moved away from the family, lost their job, were rejected or disapproved of by the community, suffered a serious illness, lost a family member (death of husband/wife/common-law spouse) or lost a relative (death of father/mother/family member when they were under the age of 12 years). A favourable answer (yes) was coded as 1 for each of these events (on scores between 0 and 7). The variable 'recent stress events' was dichotomized, meaning that the subject either experienced stress or not (score = 0). The final models satisfied collinearity criteria. Statistical analyses were performed with the SAS for Windows statistical software package version 9 (SAS Institute, Inc., Cary, NC, USA). Differences between groups and associations were considered significant at $P < 0{\cdot}05$ (bilateral).

Results

Table 2 reports study subject characteristics according to high-level PD. The prevalence of high-level PD in this population was 17·9 %. Mean age of the participants was 35·2 (SD 13·9) years. A higher proportion of younger, single and more educated subjects were in the high-level PD category. Figure 1 shows EPA + DHA plasma PL

Table 2 Characteristics of the study subjects (%) according to high-level psychological distress (PD): James Bay Cree Indian adults aged 18 years and over (*n* 852)

	High-level PD*		
	Yes (*n* 154)	No (*n* 698)	*P* value
Age (years)			<0·0001
18–24	42·9	23·5	
25–44	50·7	43·8	
≥45	6·5	32·7	
Female	60·6	52·1	0·0538
Total plasma cholesterol <5·2 (mmol/l)	81·5	65·7	0·0002
Single	44·4	29·3	0·0003
More than elementary school education	84·4	57·3	<0·0001
Unemployed†	18·0	13·2	0·1213
≥1 chronic medical illness in lifetime	42·0	55·0	0·0032
Recent stress events	54·3	44·6	0·0305
Smoking status			0·0006
Never smoked	3·5	8·9	
Ex-smokers	32·4	43·0	
Smokers‡	64·2	48·1	
Used drugs in lifetime§	64·6	35·0	<0·0001
CAGE score ≥2‖	58·0	37·4	<0·0001
BMI (kg/m^2)¶			0·7634
<25	15·6	17·8	
25–30	35·3	33·2	
≥30	49·2	48·9	

*Participants were included as high-level PD if they scored over the 80th percentile of the PD Index Santé-Québec Survey (PDISQS-14). Non-distressed participants were those scoring less than this cut-off.
†The unemployed group combined those receiving unemployment insurance or welfare, looking for a job and unemployed. The remunerated employment group combined professionals, executives, white- and blue-collar workers, trappers, houseworkers and independent workers.
‡Combined regular and occasional smokers.
§Combined users and ex-users of marijuana, hashish, cocaine, substance sniffing (solvents, glue, gasoline) and other illicit drugs. To be considered 'abstinent', subjects must never have consumed any illicit drugs.
‖CAGE (Cutting down, Annoyance by criticism, Guilty feelings, and Eye-openers) alcoholism risk questionnaire.
¶BMI is weight (kg) divided by the square of height (m^2). Only three subjects (two in the non-distressed group) had BMI < 18·5 kg/m^2.

https://doi.org/10.1017/S1368980009004935 Published online by Cambridge University Press

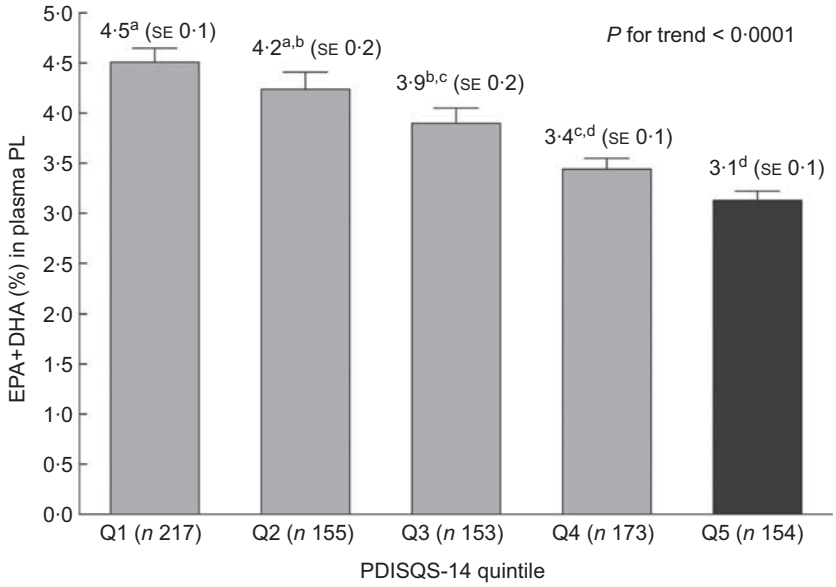

Fig. 1 Mean proportion of EPA + DHA in plasma phospholipids (PL) according to quintile of Psychological Distress Index Santé-Québec Survey (PDISQS-14) scores among James Bay Cree Indians. Higher quintiles signify higher PD scores (■, high-level PD group; ▭, non-distressed groups). Values are means with their standard errors shown by positive vertical bars. [a,b,c,d]Mean values with unlike superscript letters were significantly different (ANOVA with Bonferroni correction, $P < 0{\cdot}0025$)

Table 3 Fatty acid proportions in plasma phospholipids according to high-level psychological distress (PD): James Bay Cree Indian adults aged 18 years and over

	High-level PD				
	Yes (*n* 154)		No (*n* 698)		
Fatty acids (% of total)	Mean	SD	Mean	SD	*P* value*
Total *n*-6 PUFA†	31·9	2·3	30·8	2·7	<0·0001
LA (18 : 2*n*-6)	19·8	2·8	18·5	3·1	<0·0001
AA (20 : 4*n*-6)	8·8	1·8	9·3	1·9	0·004
Total *n*-3 PUFA‡	4·2	1·3	5·2	2·2	<0·0001
α-LNA (18 : 3*n*-3)	0·21	0·10	0·21	0·10	0·68
EPA (20 : 5*n*-3)	0·60	0·46	0·93	0·86	<0·0001
DPA*n*-3 (22 : 5*n*-3)	0·68	0·21	0·74	0·24	0·008
DHA (22 : 6*n*-3)	2·5	0·9	3·1	1·2	<0·0001
Sum EPA + DHA	3·1	1·2	4·1	2·0	<0·0001
Sum EPA + DPA*n*-3 + DHA	3·8	1·3	4·8	2·1	<0·0001
Total *n*-3/total *n*-6	0·13	0·05	0·17	0·09	<0·0001
EPA/AA	0·07	0·04	0·10	0·08	<0·0001

LA, linoleic acid; AA, arachidonic acid; α-LNA, α-linolenic acid; DPA*n*-3, docosapentaenoic acid.
**P* values were calculated for log-transformed fatty acids.
†Sum of *n*-6 PUFA (18 : 2 + 18 : 3 + 20 : 2 + 20 : 3 + 20 : 4 + 22 : 2 + 22 : 4 + 22 : 5).
‡Sum of *n*-3 PUFA (18 : 3 + 18 : 4 + 20 : 3 + 20 : 4 + 20 : 5 + 22 : 5 + 22 : 6).

proportions according to PDISQS-14 quintiles. Higher PDISQS-14 quintiles indicate higher PD scores, with the fifth quintile corresponding to the high-level PD category. A lower EPA + DHA proportion (*P* for trend <0·0001) was observed with increasing quintile of PDISQS-14 scores, especially among those categorized as high-level PD. Comparison of EPA + DHA in plasma PL between extreme PDISQS-14 quintiles, the lowest distress score category (Q1) compared with the high-level PD category (Q5), indicated a difference of 1·38% (95% CI 0·84, 1·91%). PUFA proportions in plasma PL are enumerated in Table 3. Mean proportions of *n*-3 FA, except α-LNA, were significantly lower in the PD group compared with the non-distressed group. Compared with non-distressed subjects, those with high-level PD had higher linoleic acid and lower AA proportions in their plasma PL.

Table 4 presents the OR for high-level PD according to the plasma PL tertiles of *n*-3 FA, with the lowest tertile group serving as the reference group. EPA was the only individual *n*-3 FA significantly associated with the risk of high-level PD in the multivariate model. Combinations of EPA + DHA or EPA + docosapentaenoic acid

https://doi.org/10.1017/S1368980009004935 Published online by Cambridge University Press

Table 4 Odds ratios for high-level psychological distress (PD) according to tertile of *n*-3 fatty acids (FA) in plasma phospholipids: James Bay Cree Indian adults aged 18 years and over

	High-level PD		Crude		Model 1*		Model 2†	
FA tertile: median (range)	No (*n*)	Yes (*n*)	OR	95 % CI	OR	95 % CI	OR	95 % CI
α-LNA								
T1: 0·14 (0–0·17)	236	47	1·00		1·00		1·00	
T2: 0·20 (0·17–0·23)	232	52	1·13	0·73, 1·75	1·11	0·71, 1·74	1·16	0·73, 1·83
T3: 0·28 (0·23–0·97)	230	55	1·20	0·78, 1·85	1·16	0·74, 1·82	1·17	0·73, 1·86
P for trend			0·4097		0·5186			0·5113
EPA								
T1: 0·36 (0–0·45)	221	62	1·00		1·00		1·00	
T2: 0·58 (0·45–0·81)	215	69	1·13	0·77, 1·68	1·33	0·89, 2·00	1·42	0·93, 2·15
T3: 1·32 (0·81–7·35)	262	23	0·29	0·17, 0·49	0·53	0·31, 0·93	0·56	0·32, 0·99
P for trend			<0·0001		0·0321			0·0535
DPA*n*-3								
T1: 0·54 (0–0·62)	217	66	1·00		1·00		1·00	
T2: 0·69 (0·62–0·78)	239	45	0·63	0·42, 0·97	0·79	0·51, 1·22	0·77	0·49, 1·20
T3: 0·92 (0·78–2·05)	242	43	0·56	0·36, 0·86	1·07	0·67, 1·71	1·13	0·70, 1·84
P for trend			0·0079		0·8487			0·6732
DHA								
T1: 1·95 (0·71–2·40)	210	73	1·00		1·00		1·00	
T2: 2·81 (2·40–3·32)	231	53	0·66	0·44, 0·98	0·79	0·52, 1·20	0·84	0·55, 1·28
T3: 4·14 (3·32–8·20)	257	28	0·29	0·18, 0·48	0·57	0·34, 0·97	0·65	0·38, 1·12
P for trend			<0·0001		0·0356			0·1146
Sum EPA + DHA								
T1: 2·33 (0·88–2·87)	212	72	1·00		1·00		1·00	
T2: 3·42 (2·87–4·10)	226	57	0·72	0·49, 1·07	0·85	0·57, 1·28	0·89	0·59, 1·36
T3: 5·49 (4·10–13·77)	260	25	0·26	0·16, 0·42	0·50	0·29, 0·87	0·56	0·32, 0·98
P for trend			<0·0001		0·0173			0·0495
Sum EPA + DPA*n*-3 + DHA								
T1: 2·95 (1·03–3·48)	209	75	1·00		1·00		1·00	
T2: 4·10 (3·48–4·86)	231	53	0·63	0·43, 0·94	0·75	0·50, 1·13	0·79	0·52, 1·20
T3: 6·37 (4·87–14·67)	258	26	0·25	0·15, 0·41	0·50	0·29, 0·86	0·55	0·32, 0·97
P for trend			<0·0001		0·0112			0·0368
Total *n*-3 PUFA								
T1: 3·28 (1·25–3·84)	196	73	1·00		1·00		1·00	
T2: 4·47 (3·85–5·29)	244	55	0·61	0·41, 0·90	0·71	0·47, 1·07	0·75	0·49, 1·14
T3: 6·83 (5·30–15·00)	258	26	0·24	0·15, 0·40	0·47	0·27, 0·82	0·52	0·30, 0·92
P for trend			<0·0001		0·0059			0·0207

α-LNA, α-linolenic acid (18 : 3*n*-3); EPA, 20 : 5*n*-3; DPA*n*-3, docosapentaenoic acid (22 : 5*n*-3); DHA, 22 : 6*n*-3; total *n*-3, sum of *n*-3 PUFA (18 : 3 + 18 : 4 + 20 : 3 + 20 : 4 + 20 : 5 + 22 : 5 + 22 : 6).
*Multivariate model 1 controlled for age and gender.
†Multivariate model 2 included the variables in multivariate model 1 and smoking status, recent stress events, education, total plasma cholesterol and chronic medical illness.

(DPA*n*-3) + DHA or the sum of *n*-3 were all associated with the risk of high-level PD. Compared with the lowest EPA + DHA tertile (median = 2·3), the model adjusted for age and sex indicated that the OR for high-level PD was 0·85 (95 % CI 0·57, 1·28) for the second tertile (median = 3·4) and 0·50 (95 % CI 0·29, 0·87) for the third tertile (median = 5·5). After controlling for confounders in the multivariate model, the OR for high-level PD was 0·89 (95 % CI 0·59, 1·36) for the second tertile and 0·56 (95 % CI 0·32, 0·98) for the third tertile, compared with the lowest EPA + DHA tertile.

Discussion

In the present cross-sectional study, we noted significantly lower plasma content of EPA, DPA*n*-3 and DHA among subjects categorized as high-level PD compared with non-distressed subjects. After adjustment for confounders, EPA was the only individual *n*-3 FA significantly associated with the risk of high-level PD. Combinations of EPA + DHA or EPA + DPA*n*-3 + DHA, or the sum of *n*-3, were also associated with the risk of high-level PD. Subjects in the third tertile of EPA + DHA in plasma PL had 1·8 times lower risk of having a high-level PD score compared with those in the lowest tertile.

Our results are in line with previous cross-sectional studies that reported an inverse relationship between fish consumption and depression[45–48]. In a cross-sectional analysis of *n*-3 plasma PL and PDISQS-14 among Nunavik Inuit, we recently noted that women in the second and third tertiles of EPA + DHA proportions in plasma PL had three times lower risk of a high-level PD score than women in the lowest tertile[49]. However, we did not

https://doi.org/10.1017/S1368980009004935 Published online by Cambridge University Press

observe this difference among men. In the Hordaland Health Study, users of cod-liver oil were less likely than non-users to have high levels of depressive symptoms on the Hospital Anxiety and Depression Scale, but not high levels of anxiety symptoms[50]. In 771 patients with newly diagnosed lung cancer, Suzuki *et al.* reported no association between EPA + DHA intake and the Depression Subscale of the Hospital Anxiety and Depression Scale (cut-off ≥5)[51]. However, they recorded a two times lower risk ($P < 0{\cdot}05$) in the fourth quartile of α-LNA intake compared with the first quartile. In our analyses, we did not see a relationship between α-LNA and PDISQS-14 scores. In a cross-sectional investigation of data from a nationally representative sample of 4644 New Zealand adults, Silvers and Scott[52] demonstrated that higher fish consumption was associated with higher self-reported mental health status.

Except for EPA, no individual *n*-3 FA was significantly associated with risk of high-level PD in the multivariate model. These results are in line with Three-City Study findings[48]. Cross-sectional analyses indicated that only plasma EPA, and not DHA, was inversely associated with the severity of depressive symptomatology among 1390 elderly French subjects. Some authors argue that studies of EPA alone or with a higher ratio of EPA to DHA are associated with better outcomes than trials of an enriched DHA supplement[33,53]. Our results might also be explained by the fact that EPA in blood appears to be less saturable than DHA[54,55]. Brown *et al.*[56] suggested that DHA turnover in red blood cells (RBC) is slower than EPA. However, others have noted stronger correlations between fish intake and plasma DHA than EPA[57,58]. Nevertheless, it has been postulated that the combination of EPA and DHA may be a better independent variable to assess the health effects of *n*-3 LC PUFA consumption[59].

To date, two cohort studies have prospectively analysed the association between *n*-3 intake and fish consumption and mental disorders[60,61]. The first, a longitudinal trial among 29 133 Finnish men, failed to find an association between *n*-3 from fish and self-reported depressed mood or hospital treatment for major depression[60]. However, several limitations could explain these negative results[15]. In the second, the SUN (Seguimiento University of Navarra) cohort study, only the fourth quintile of baseline *n*-3 LC PUFA intake was significantly associated with a lower risk of incident mental disorder (defined as self-reported physician diagnosis of depression, anxiety or stress or the use of antidepressant medications or tranquilizers). No linear trend was apparent between baseline *n*-3 LC PUFA intake and incident mental disorder after 2 years of follow-up. However, compared with the Structured Clinical Interview for DSM-IV, physician recognition of major depressive episode was poor (sensitivity = 40 %)[62]. Moreover, the rates of untreated mental disorders are high in different countries[63]. Therefore, antidepressant medications and tranquilizers are also poor indicators of mental disorder. In addition, *n*-3 LC PUFA intakes were very high in this cohort. The first and fifth quintiles of median energy-adjusted *n*-3 LC PUFA intakes were respectively 0·39 and 1·89 g/d.

Our results must be interpreted in the context of the limitations and strengths of any cross-sectional study. As a consequence, we cannot ascertain any causal relationship and we cannot rule out the possibility that higher PD (especially if it was characterized by depression) influenced *n*-3 LC PUFA intakes from fish. A recent meta-analysis of double-blind, placebo-controlled studies has suggested that *n*-3 LC PUFA significantly improve symptoms in patients with clearly defined depression[64]. However, no major clinical investigation has been published, and the most significant trials tested *n*-3 LC PUFA supplementation as an adjunct to antidepressant therapy. Moreover, two recent meta-analyses on *n*-3 LC PUFA and depression noted significant heterogeneity and publication bias[64,65]. A weakness of our study is that the PDISQS-14 cannot be used to ascertain specific psychiatric disorders. However, the present analysis did not aim to assess the prevalence of specific psychiatric disorders but rather to identify if *n*-3 LC PUFA could be associated with the global index of PD. Even though severe PD cannot be directly expressed in terms of clinical psychiatric disorders, we can, however, postulate that the risk of psychopathology increases with the level of PD. It is possible that the outcomes noted in the PDISQS-14 were due to *n*-3 LC PUFA effects not only on depression but also on anxiety and hostility items. However, the literature on the relationship between *n*-3 LC PUFA and anxiety and hostility is less abundant than for depression. Indeed, some studies show the benefits of *n*-3 LC PUFA in anxiety disorders[66,67] but others do not[50,68]. A role of *n*-3 LC PUFA has been suggested in disorders characterized by impulsivity[69]. However, in a recent randomized controlled trial among patients with recurrent self-harm, EPA + DHA supplementation did not improve impulsivity, aggression or hostility[70].

A single assessment of *n*-3 LC PUFA in blood reflects the ranking of *n*-3 LC PUFA intakes from fish[71]. Such biomarkers of FA intakes provide quantitative measurements independently of memory and/or knowledge of the subjects and are less likely to be due to social desirability bias than dietary self-reporting[72]. It is likely that our correlations might be influenced by the utilization of plasma PL rather than RBC analysis. Indeed, plasma PL FA determination reflects short-term intake better than RBC. According to the 18-month controlled study of Katan *et al.*, half-maximal and maximal concentrations of EPA in RBC were reached after 28 and 180 d[73]. However, these stages were attained after 4·8 and 56 d for serum cholesteryl esters, indicating that RBC might reflect long-term intake better than plasma or serum. However, correlations between plasma PL and RBC DHA and EPA are strong[54,74]. Moreover, analysis of plasma EPA + DHA is

not only a measure of traditional food consumption but also a yardstick for adherence to traditional behaviours such as fishing and hunting. It is, therefore, difficult to separate the biological effect of social behaviour adherence to Cree culture when EPA + DHA are measured. Furthermore, illicit drugs and alcohol consumption were not added in our multivariate model since these variables could be surrogate markers of PD and would lead to over-adjustment.

Conclusion

In the present retrospective cross-sectional study, we found that *n*-3 LC PUFA proportions in plasma PL, a marker of *n*-3 LC PUFA consumption from fish, were inversely associated with PD. These observations are consistent with other investigations indicating an effect of *n*-3 LC PUFA in mood disorders. However, the causal relationship between *n*-3 LC PUFA in plasma PL and mood in this population should be established prospectively.

Acknowledgements

The study was supported by Indian and Northern Affairs Canada. No authors have reported financial disclosures or conflicts of interest related to the present manuscript. The contributions of each author in this work are as follows: study concept and design – E.D., C.B., S.G. and M.L.; analysis of the data – M.L., E.D., S.G. and C.B.; interpretation of the data – M.L., E.D., C.B., S.G. and B.J.H.; drafting the manuscript – M.L. and E.D.; critical revision of the manuscript – M.L., E.D., C.B., S.G. and B.J.H. The authors acknowledge the close cooperation of Santé-Québec in providing access to health survey databases on the James Bay Cree. The authors also express their gratitude to the Cree Board of Health and Social Services of James Bay and to all participants in the Santé-Québec Health Survey.

References

1. Kirmayer LJ, Brass GM & Tait CL (2000) The mental health of Aboriginal peoples: transformations of identity and community. *Can J Psychiatry* **45**, 607–616.
2. McGrath-Hanna NK, Greene DM, Tavernier RJ & Bult-Ito A (2003) Diet and mental health in the Arctic: is diet an important risk factor for mental health in circumpolar peoples? A review. *Int J Circumpolar Health* **62**, 228–241.
3. Boothroyd LJ, Kirmayer LJ, Spreng S, Malus M & Hodgins S (2000) Completed suicides among the Inuit of northern Quebec, 1982–1996: a case–control study. *CMAJ* **165**, 749–755.
4. Waldram JB, Herring DA & Young TK (2006) *Aboriginal Health in Canada: Historical, Cultural, and Epidemiological Perspectives*, 2nd ed. Toronto: University of Toronto Press.
5. Kirmayer LJ, Macdonald ME & GM Brass (2000) *The Mental Health of Indigenous Peoples. Report* no. 10. Montreal: Culture & Mental Health Research Unit, Institute of Community & Family Psychiatry, Sir Mortimer B. Davis–Jewish General Hospital.
6. Chandler MJ & Lalonde C (1998) Cultural continuity as a hedge against suicide in Canada's First Nations. *Transcult Psychiatry* **35**, 191–219.
7. Haggarty J, Cernovsky Z, Kermeen P & Merskey H (2000) Psychiatric disorders in an Arctic community. *Can J Psychiatry* **45**, 357–362.
8. Lavallée C, Robinson E & Laverdure J (1991) Description of customers and services of mental health among the Cree people (North Quebec). *Sante Cult* **8**, 265–284.
9. Santé-Québec, Daveluy C & Bertrand L (editors) (1998) *A Dietary Profile of the Cree: Report of the Santé Québec Health Survey of the James Bay Cree, 1991: Food and Nutrient Intake*. Montréal: Ministère de la santé et des services sociaux, Government of Quebec.
10. Santé Québec, Daveluy C, Lavallée C, Clarkson M & Robinson E (editors) (1994) *A Health Profile of the Cree: Report of the Santé Québec Health Survey of the James Bay Cree 1991*. Montréal: Ministère de la santé et des services sociaux, Government of Quebec.
11. Prince RH (1993) Psychiatry among the James Bay Cree: a focus on pathological grief reactions. *Transcult Psychiatry Res Rev* **30**, 3–50.
12. Dewailly E, Blanchet C, Gingras S, Lemieux S & Holub BJ (2002) Cardiovascular disease risk factors and *n*-3 fatty acid status in the adult population of James Bay Cree. *Am J Clin Nutr* **76**, 85–92.
13. Hibbeln JR & Salem N Jr (1995) Dietary polyunsaturated fatty acids and depression: when cholesterol does not satisfy. *Am J Clin Nutr* **62**, 1–9.
14. Parker G, Gibson NA, Brotchie H, Heruc G, Rees AM & Hadzi-Pavlovic D (2006) Omega-3 fatty acids and mood disorders. *Am J Psychiatry* **163**, 969–978.
15. Sontrop J & Campbell MK (2006) Omega-3 polyunsaturated fatty acids and depression: a review of the evidence and a methodological critique. *Prev Med* **42**, 4–13.
16. Plourde M & Cunnane S (2007) Extremely limited synthesis of long chain polyunsaturates in adults: implications for their dietary essentiality and use as supplements. *Appl Physiol Nutr Metab* **32**, 619–634.
17. Kobayashi M, Sasaki S, Kawabata T, Hasegawa K & Tsugane S (2003) Validity of a self-administered food frequency questionnaire used in the 5-year follow-up survey of the JPHC Study Cohort I to assess fatty acid intake: comparison with dietary records and serum phospholipid level. *J Epidemiol* **13**, 1 Suppl., S64–S81.
18. Kuriki K, Nagaya T, Tokudome Y *et al.* (2003) Plasma concentrations of (*n*-3) highly unsaturated fatty acids are good biomarkers of relative dietary fatty acid intakes: a cross-sectional study. *J Nutr* **133**, 3643–3650.
19. Hjartaker A, Lund E & Bjerve KS (1997) Serum phospholipid fatty acid composition and habitual intake of marine foods registered by a semi-quantitative food frequency questionnaire. *Eur J Clin Nutr* **51**, 736–742.
20. Yehuda S, Rabinovitz S & Mostofsky DI (1999) Essential fatty acids are mediators of brain biochemistry and cognitive functions. *J Neurosci Res* **56**, 565–570.
21. Martinez M (1992) Tissue levels of polyunsaturated fatty acids during early human development. *J Pediatr* **120**, s129–s138.
22. McNamara RK & Carlson SE (2006) Role of omega-3 fatty acids in brain development and function: potential implications for the pathogenesis and prevention of psychopathology. *Prostaglandins Leukot Essent Fatty Acids* **75**, 329–349.
23. Delion S, Chalon S, Guilloteau D, Besnard JC & Durand G (1996) α-Linolenic acid dietary deficiency alters age-related changes of dopaminergic and serotoninergic neurotransmission in the rat frontal cortex. *J Neurochem* **66**, 1582–1591.

24. Delion S, Chalon S, Guilloteau D, Lejeune B, Besnard JC & Durand G (1997) Age-related changes in phospholipid fatty acid composition and monoaminergic neurotransmission in the hippocampus of rats fed a balanced or an *n*-3 polyunsaturated fatty acid-deficient diet. *J Lipid Res* **38**, 680–689.
25. Delion S, Chalon S, Hérault J, Guilloteau D, Besnard J-C & Durand G (1994) Chronic dietary α-linolenic acid deficiency alters dopaminergic and serotoninergic neurotransmission in rats. *J Nutr* **124**, 2466–2476.
26. de la Presa Owens S & Innis SM (1999) Docosahexaenoic and arachidonic acid prevent a decrease in dopaminergic and serotoninergic neurotransmitters in frontal cortex caused by a linoleic and α-linolenic acid deficient diet in formula-fed piglets. *J Nutr* **129**, 2088–2093.
27. Kodas E, Galineau L, Bodard S, Vancassel S, Guilloteau D, Besnard JC & Chalon S (2004) Serotoninergic neurotransmission is affected by *n*-3 polyunsaturated fatty acids in the rat. *J Neurochem* **89**, 695–702.
28. Hibbeln JR, Umhau JC, Linnoila M, George DT, Ragan PW, Shoaf SE, Vaughan MR, Rawlings R & Salem N Jr (1998) A replication study of violent and nonviolent subjects: cerebrospinal fluid metabolites of serotonin and dopamine are predicted by plasma essential fatty acids. *Biol Psychiatry* **44**, 243–249.
29. Hibbeln JR, Linnoila M, Umhau JC, Rawlings R, George DT & Salem N Jr (1998) Essential fatty acids predict metabolites of serotonin and dopamine in cerebrospinal fluid among healthy control subjects, and early- and late-onset alcoholics. *Biol Psychiatry* **44**, 235–242.
30. Serhan CN (2005) Novel omega-3 derived local mediators in anti-inflammation and resolution. *Pharmacol Ther* **105**, 7–21.
31. Farooqui AA, Horrocks LA & Farooqui T (2007) Modulation of inflammation in brain: a matter of fat. *J Neurochem* **101**, 577–599.
32. Haag M (2003) Essential fatty acids and the brain. *Can J Psychiatry* **48**, 195–203.
33. Stahl LA, Begg DP, Weisinger RS & Sinclair AJ (2008) The role of omega-3 fatty acids in mood disorders. *Curr Opin Invest Drugs* **9**, 57–64.
34. Kirmayer LJ, Boothroyd LJ, Tanner A, Adelson N & Robinson E (2000) Psychological distress among the Cree of James Bay. *Transcult Psychiatry* **37**, 35–56.
35. Préville M, Boyer R & Potvin L (1992) *La détresse psychologique: détermination de la fiabilité et de la validité de la mesure utilisée dans l'enquête Santé Québec, enquête Santé Québec 1987. Les cahiers de recherche* no. 7. Montréal: Ministère de la santé et des services sociaux, Government of Quebec.
36. Preville M, Potvin L & Boyer R (1995) The structure of psychological distress. *Psychol Rep* **77**, 275–293.
37. Ilfeld FW Jr (1978) Psychologic status of community residents along major demographic dimensions. *Arch Gen Psychiatry* **35**, 716–724.
38. Ilfeld FW (1976) Further validation of a psychiatric symptom index in a normal population. *Psychol Rep* **39**, 1215–1228.
39. Martin F, Sabourin S & Gendreau P (1989) Les dimensions de la detresse psychologique: analyse factorielle confirmatoire de type hierarchique. *Int J Psychol* **24**, 571–584.
40. Boyer R, Preville M, Legare G & Valois P (1993) Psychological distress in a noninstitutionalized population of Quebec: normative results of the Quebec health survey. *Can J Psychiatry* **38**, 339–343.
41. Stark KD & Holub BJ (2004) Differential eicosapentaenoic acid elevations and altered cardiovascular disease risk factor responses after supplementation with docosahexaenoic acid in postmenopausal women receiving and not receiving hormone replacement therapy. *Am J Clin Nutr* **79**, 765–773.
42. Babyak MA (2004) What you see may not be what you get: a brief, nontechnical introduction to overfitting in regression-type models. *Psychosom Med* **66**, 411–421.
43. Peduzzi P, Concato J, Kemper E, Holford TR & Feinstein AR (1996) A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* **49**, 1373–1379.
44. Steyerberg EW, Eijkemans MJ, Harrell FE Jr & Habbema JD (2001) Prognostic modeling with logistic regression analysis: in search of a sensible strategy in small data sets. *Med Decis Making* **21**, 45–56.
45. Timonen M, Horrobin D, Jokelainen J, Laitinen J, Herva A & Rasanen P (2004) Fish consumption and depression: the Northern Finland 1966 birth cohort study. *J Affect Disord* **82**, 447–452.
46. Tanskanen A, Hibbeln JR, Tuomilehto J, Uutela A, Haukkala A, Viinamaki H, Lehtonen J & Vartiainen E (2001) Fish consumption and depressive symptoms in the general population in Finland. *Psychiatr Serv* **52**, 529–531.
47. Kamphuis MH, Geerlings MI, Tijhuis MA, Kalmijn S, Grobbee DE & Kromhout D (2006) Depression and cardiovascular mortality: a role for *n*-3 fatty acids? *Am J Clin Nutr* **84**, 1513–1517.
48. Feart C, Peuchant E, Letenneur L, Samieri C, Montagnier D, Fourrier-Reglat A & Barberger-Gateau P (2008) Plasma eicosapentaenoic acid is inversely associated with severity of depressive symptomatology in the elderly: data from the Bordeaux sample of the Three-City Study. *Am J Clin Nutr* **87**, 1156–1162.
49. Lucas M, Dewailly E, Blanchet B, Gingras S & Holub BJ (2009) Plasma omega-3 and psychological distress among Nunavik Inuit (Canada). *Psychiatry Res* (In the Press).
50. Raeder MB, Steen VM, Vollset SE & Bjelland I (2007) Associations between cod liver oil use and symptoms of depression: the Hordaland Health Study. *J Affect Disord* **101**, 245–249.
51. Suzuki S, Akechi T, Kobayashi M, Taniguchi K, Goto K, Sasaki S, Tsugane S, Nishiwaki Y, Miyaoka H & Uchitomi Y (2004) Daily omega-3 fatty acid intake and depression in Japanese patients with newly diagnosed lung cancer. *Br J Cancer* **90**, 787–793.
52. Silvers KM & Scott KM (2002) Fish consumption and self-reported physical and mental health status. *Public Health Nutr* **5**, 427–431.
53. Kidd PM (2007) Omega-3 DHA and EPA for cognition, behavior, and mood: clinical findings and structural–functional synergies with cell membrane phospholipids. *Altern Med Rev* **12**, 207–227.
54. Arterburn LM, Hall EB & Oken H (2006) Distribution, interconversion, and dose response of *n*-3 fatty acids in humans. *Am J Clin Nutr* **83**, 6 Suppl., 1467S–1476S.
55. Brown AJ, Pang E & Roberts DCK (1991) Erythrocyte eicosapentaenoic acid versus docosahexaenoic acid as a marker for fish and fish oil consumption. *Prostaglandins Leukot Essent Fatty Acids* **44**, 103–106.
56. Brown AJ, Pang E & Roberts DC (1991) Persistent changes in the fatty acid composition of erythrocyte membranes after moderate intake of *n*-3 polyunsaturated fatty acids: study design implications. *Am J Clin Nutr* **54**, 668–673.
57. Mina K, Fritschi L & Knuiman M (2007) A valid semiquantitative food frequency questionnaire to measure fish consumption. *Eur J Clin Nutr* **61**, 1023–1031.
58. Woods RK, Stoney RM, Ireland PD, Bailey MJ, Raven JM, Thien FC, Walters EH & Abramson MJ (2002) A valid food frequency questionnaire for measuring dietary fish intake. *Asia Pac J Clin Nutr* **11**, 56–61.
59. Harris WS & Von Schacky C (2004) The Omega-3 Index: a new risk factor for death from coronary heart disease? *Prev Med* **39**, 212–220.

60. Hakkarainen R, Partonen T, Haukka J, Virtamo J, Albanes D & Lonnqvist J (2004) Is low dietary intake of omega-3 fatty acids associated with depression? *Am J Psychiatry* **161**, 567–569.
61. Sanchez-Villegas A, Henriquez P, Figueiras A, Ortuno F, Lahortiga F & Martinez-Gonzalez MA (2007) Long chain omega-3 fatty acids intake, fish consumption and mental disorders in the SUN cohort study. *Eur J Nutr* **46**, 337–346.
62. Lowe B, Spitzer RL, Grafe K, Kroenke K, Quenter A, Zipfel S, Buchholz C, Witte S & Herzog W (2004) Comparative validity of three screening questionnaires for DSM-IV depressive disorders and physicians' diagnoses. *J Affect Disord* **78**, 131–140.
63. Bijl RV, de Graaf R, Hiripi E *et al.* (2003) The prevalence of treated and untreated mental disorders in five countries. *Health Aff (Millwood)* **22**, 122–133.
64. Lin PY & Su KP (2007) A meta-analytic review of double-blind, placebo-controlled trials of antidepressant efficacy of omega-3 fatty acids. *J Clin Psychiatry* **68**, 1056–1061.
65. Appleton KM, Hayward RC, Gunnell D, Peters TJ, Rogers PJ, Kessler D & Ness AR (2006) Effects of *n*-3 long-chain polyunsaturated fatty acids on depressed mood: systematic review of published trials. *Am J Clin Nutr* **84**, 1308–1316.
66. Green P, Hermesh H, Monselise A, Marom S, Presburger G & Weizman A (2006) Red cell membrane omega-3 fatty acids are decreased in nondepressed patients with social anxiety disorder. *Eur Neuropsychopharmacol* **16**, 107–113.
67. Buydens-Branchey L & Branchey M (2006) *n*-3 Polyunsaturated fatty acids decrease anxiety feelings in a population of substance abusers. *J Clin Psychopharmacol* **26**, 661–665.
68. Fux M, Benjamin J & Nemets B (2004) A placebo-controlled cross-over trial of adjunctive EPA in OCD. *J Psychiatr Res* **38**, 323–325.
69. Hallahan B & Garland MR (2004) Essential fatty acids and their role in the treatment of impulsivity disorders. *Prostaglandins Leukot Essent Fatty Acids* **71**, 211–216.
70. Hallahan B, Hibbeln JR, Davis JM & Garland MR (2007) Omega-3 fatty acid supplementation in patients with recurrent self-harm. Single-centre double-blind randomised controlled trial. *Br J Psychiatry* **190**, 118–122.
71. Kobayashi M, Sasaki S, Kawabata T, Hasegawa K, Akabane M & Tsugane S (2001) Single measurement of serum phospholipid fatty acid as a biomarker of specific fatty acid intake in middle-aged Japanese men. *Eur J Clin Nutr* **55**, 643–650.
72. Hebert JR, Ma Y, Clemow L, Ockene IS, Saperia G, Stanek EJ 3rd, Merriam PA & Ockene JK (1997) Gender differences in social desirability and social approval bias in dietary self-report. *Am J Epidemiol* **146**, 1046–1055.
73. Katan MB, Deslypere JP, van Birgelen APJM, Penders M & Zegwaard M (1997) Kinetics of the incorporation of dietary fatty acids into serum cholesteryl esters, erythrocyte membranes, and adipose tissue: an 18-month controlled study. *J Lipid Res* **38**, 2012–2022.
74. Sun Q, Ma J, Campos H, Hankinson SE & Hu FB (2007) Comparison between plasma and erythrocyte fatty acid content as biomarkers of fatty acid intake in US women. *Am J Clin Nutr* **86**, 74–81.