

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

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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

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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 $\approx 80\%$ 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

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.

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 $\alpha = 0.94$)⁽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.

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 ($P < 0.0025$) 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 $P < 0.05$ (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*		<i>P</i> value
	Yes (<i>n</i> 154)	No (<i>n</i> 698)	
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 .

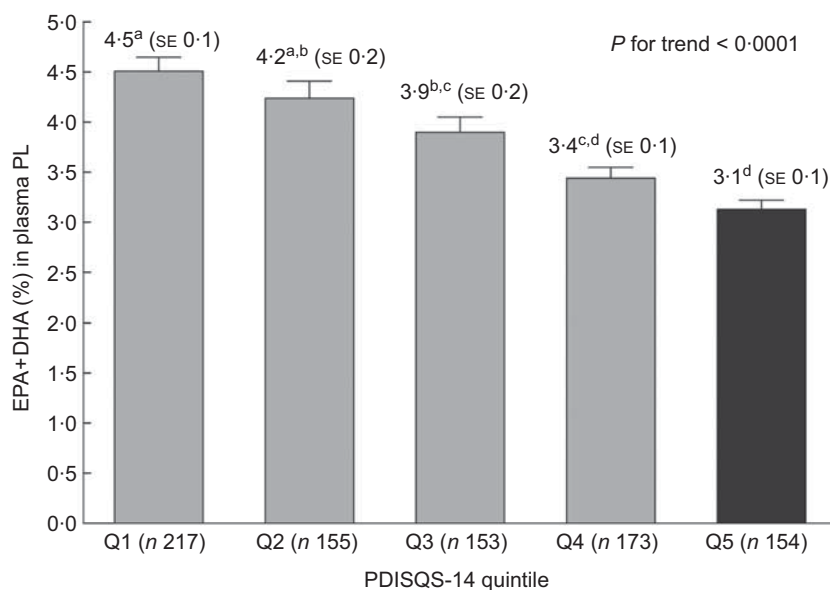


Fig. 1 Mean proportion of EPA + DHA in plasma phospholipids (PL) according to quintile of Psychological Distress Index Santé-Québec Survey (PDISQS-14) scores among James Bay Cree Indians. Higher quintiles signify higher PD scores (■, high-level PD group; □, non-distressed groups). Values are means with 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, $P < 0.0025$)

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

Fatty acids (% of total)	High-level PD				P value*
	Yes (n 154)		No (n 698)		
	Mean	SD	Mean	SD	
Total <i>n</i> -6 PUFA†	31.9	2.3	30.8	2.7	<0.0001
LA (18:2 <i>n</i> -6)	19.8	2.8	18.5	3.1	<0.0001
AA (20:4 <i>n</i> -6)	8.8	1.8	9.3	1.9	0.004
Total <i>n</i> -3 PUFA‡	4.2	1.3	5.2	2.2	<0.0001
α-LNA (18:3 <i>n</i> -3)	0.21	0.10	0.21	0.10	0.68
EPA (20:5 <i>n</i> -3)	0.60	0.46	0.93	0.86	<0.0001
DPA <i>n</i> -3 (22:5 <i>n</i> -3)	0.68	0.21	0.74	0.24	0.008
DHA (22:6 <i>n</i> -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 <i>n</i> -3 + DHA	3.8	1.3	4.8	2.1	<0.0001
Total <i>n</i> -3/total <i>n</i> -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

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

FA tertile: median (range)	High-level PD		Crude		Model 1*		Model 2†	
	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 (18:3n-3); EPA, 20:5n-3; DPA n-3, docosapentaenoic acid (22:5n-3); DHA, 22:6n-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

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 ($P < 0.05$) 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 29133 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.

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