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People with schizophrenia and depression have a low omega-3 index

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ABSTRACT

Cardiovascular disease (CVD) is higher in people with mental illness and is associated with a 30 year higher mortality rate in this population. Erythrocyte docosahexaenoic acid (DHA) plus eicosapentaenoic acid (EPA) (omega-3 index) $\leq 4\%$ is a marker for increased mortality risk from CVD while $>8\%$ is protective. Omega-3 polyunsaturated fatty acids are also important for brain function and may ameliorate symptoms of mental illness. We investigated the erythrocyte omega-3 index in people with mental illness. One hundred and thirty adults aged 18–65 years (32.6% male) with schizophrenia (n=14) and depression (n=116) provided blood samples and completed physiological assessments and questionnaires. Both populations had risk factors for metabolic syndrome and CVD. The average omega-3 index was 3.95% (SD=1.06), compared to an estimated 5% in the Australian population. These data indicate an unfavourable omega-3 profile in people with mental illness that could contribute to higher CVD risk.

1. Introduction

In 2001 the World Health Organisation reported that around 450 million people worldwide suffered from a mental health problem and that one in four people will experience mental illness at some stage in their life [1]. Recent findings from the World Health Organisation's World Mental Health survey identified that mental disorders are common across 28 participating countries, with an interquartile range from 18.1% to 36.1% of lifetime prevalence [2]. Like physical health, mental health is a complex interaction of biological, psychological and social factors [1]. Not only does chronic mental illness lead to substantially reduced quality of life, social and economic burden, it is compounded by high rates of physical illness. People with serious mental illness (SMI) are more likely to suffer from a range of physical health problems, particularly metabolic syndrome/diabetes and cardiovascular disease (CVD) [3–6]. Behavioural factors that lead to poor lifestyle choices such as smoking, diet and low physical activity contribute to this higher risk [1,7]. Although medications also contribute to CVD risk factors, lifestyle factors such as poor diet (e.g. low fibre, high fat, high sugar) have been identified as independent contributors [8–10].

These lifestyle behaviours may contribute to common underlying biological mechanisms for both physical and mental illness and their comorbidities [11]. Supporting evidence comes from a meta-analysis of epidemiological studies showing a significant association between depression and metabolic syndrome [6], a cluster of risk factors for CVD including hyperglycemia and/or insulin resistance, hypertension, abdominal adiposity and hyperlipidemia. Interestingly, prospective studies identified in the latter review showed that the association is bidirectional. Another meta-analysis showed that depressed adults have a 37% increased risk of developing diabetes [5]. These studies provide evidence that people don't develop depression as a result of being physical ill, and that in fact there may be underlying mechanisms that manifest as mental illness before symptoms of physical illness become apparent.

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One of the possible common contributors to both cardiometabolic and mental health is the group of omega-3 long chain polyunsaturated fatty acids (n-3 LCPUFAs). The benefits of n-3 LCPUFA for cardiovascular health have been well established [12] (despite recent studies which are plagued by methodological issues, largely associated with the fact that they were conducted after 2000 and 2002 American Heart Foundation recommendations for increased fish and fish oil intake respectively, and subsequent exponential increase in fish oil imports [13,14]). Mechanisms for reducing CVD risk may include reduction of ventricular arrhythmia, thrombosis, triglycerides, atherosclerotic plaque, inflammation and hypertension, and endothelial relaxation [15]. Based on the body of evidence, an omega-3 index for cardiovascular health was developed by Harris and von Schacky [16]. They first established erythrocyte levels of the long chain n-3 LCPUFAs eicosapentaenoic acid (EPA; 20:5n-3) plus docosahexaenoic acid (DHA; 22:6n-3) as a valid biomarker of omega-3 status. Then by pooling together results from a body of large prospective and randomised controlled trials they identified that a combination of EPA plus DHA levels of $\leq 4\%$ in erythrocyte membranes was associated with the highest risk of mortality from coronary heart disease (CHD) whereas levels $\geq 8\%$ conferred the greatest cardioprotection. Therefore the omega-3 index was proposed as a useful biomarker to estimate risk of mortality from CHD and provide targets for reducing mortality risk.

Since the prevalence of n-3 LCPUFA DHA in brain tissue was discovered in the 1970s [17] a number of pivotal roles have been identified for DHA in brain function, including a key structural role in brain cells and phospholipids, neurite growth, membrane fluidity, neurotransmission (e.g. synthesis of neurotransmitters serotonin and dopamine), endothelial function and brain barrier integrity, neuronal survival and protection from neurodegeneration [18]. The role of EPA and DHA in improving endothelial function via production of anti-inflammatory eicosanoids, reducing adhesion of substances to the endothelial wall and influence on nitric oxide production (and therefore vasodilation and blood flow) may contribute to common underlying mechanisms for their protective role in cardiovascular and mental health [19]. A growing body of work has investigated the role of n-3 LCPUFAs in mental health with indications of benefit across the lifespan including developmental disorders, depression, schizophrenia and cognitive decline [20,21]. Following the latter studies reviewed, a robust multi-centre trial reported that n-3 LCPUFA supplementation for 12 weeks was able to significantly reduce transition to psychosis at 12 month follow-up compared to placebo in young people at high risk for psychosis [22]. We previously proposed an omega-3 index for mental health although there were as yet insufficient blood fatty acid data to establish this [23].

Inflammation has been proposed as a possible mediating role for comorbid physical and mental illness [24–28] and may be one of the mechanisms by which n-3 PUFA exert their effects. The anti-inflammatory properties of eicosanoids produced by EPA counteract the largely inflammatory properties of eicosanoids produced by arachidonic acid (AA) from the n-6 PUFA series. The n-3 and n-6 PUFA series compete for the same enzymes for elongation and desaturation, and a higher intake of one can displace the other in cell membranes. This is of concern in Western societies that have increased the intake of n-6 PUFA via vegetable oils and processed foods while decreasing intake of n-3 PUFA from nuts, seeds, dark leafy vegetables and fatty fish, including Australia [29,30]. It has been proposed therefore that the ratio of n-6/n-3 PUFAs, which in Western diets is estimated at 15-16/1 (8/1 in Australia [30]) compared to an equal ratio in traditional diets, contributes to pro-inflammatory states that underlie chronic illness [31].

In the present study we investigated erythrocyte PUFA levels in people with SMI to determine their erythrocyte omega-3 index and associations with physical and mental health. This study utilised baseline data from two related studies: a pilot study with residents of a Community Rehabilitation Centre for people with serious mental illness and a randomised controlled trial with community dwelling people suffering from depression.

2. Method

Study 1 was a partnership between the University of South Australia and the Mental Health Directorate in the Southern Adelaide Local Health Network. Ethics approval was obtained from the Southern Adelaide Clinical Human Research Ethics Committee (HREC) and the HREC at the University of South Australia. For study 2 community dwelling adults suffering depressive symptoms were recruited, for which ethics approval was provided by the HREC at the University of South Australia. Both studies aimed to investigate the effect of a Mediterranean-style diet and fish oil supplementation on cardiometabolic and mental health (HELFIMED: Healthy Eating for Life with a Mediterranean-style Diet), the first as a pilot feasibility study [32] and the second as a randomised controlled trial [33]. This report utilises baseline data from those studies. For study 1 information sessions were conducted to explain the project to staff and residents of a Community Rehabilitation Centre (CRC) with 20 beds for people with serious mental illness. The population is transient with an average stay of around 9 months. Ongoing recruitment was undertaken for the pilot feasibility study from May 2013 to February 2014 and was open to all new residents entering the CRC during that time. All consenting residents were eligible to take part. For study 2 we recruited community dwelling people via newspaper advertisements, media releases, social media and a recruitment agency. Inclusion criteria were depressive symptoms over the past 3 months or more, age between 18 and 65, poor diet according to an adapted dietary screening tool and not consuming fish oil supplements over the past 3 months.

2.1. Participants

Over an 8-month period, 25 CRC residents aged 18–59 years with schizophrenia signed up for study 1 and completed baseline assessments. In the first batch of blood samples many were oxidised due to an inappropriate protocol for washing of the red blood cells which was then rectified. Therefore, 14 blood samples were available for analysis of erythrocyte fatty acids. In study 2, 164 participants aged 18–65 completed baseline assessments. Of those, 116 people had either diagnosed depression (n = 75; 58%) and/or depressive symptoms in the 'severe' or 'extremely severe' range on the Depression, Anxiety, Stress Scale (DASS-21) [34] and are included in these analyses. Summary characteristics are provided in Table 1.

2.2. Assessments

Baseline assessments included fasted blood samples, weight, height, waist circumference and blood pressure, and the following questionnaires: the Assessment of Quality of Life (AQoL)-8D scale [35] in both studies and the DASS-21 [34] and Positive and Negative Affect Scale (PANAS) in study 2. These are described below. A background questionnaire measured the following potential covariates: age, gender, socio-economic status (Socio-Economic Indexes for Areas decile), education level (1 = completed primary school; 8 = postgraduate degree), household income, physical activity (calculated as total minutes per week), smoking status (1 = never smoked; 5 = smoke daily), and frequency of consuming >2 alcoholic drinks per day (1 = never/rarely; 5 = daily).