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Reduced Consumption of Olive Oil: A Risk for Ischemic Heart Disease?

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Additional information is available at the end of the chapter

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1. Introduction

Comparing the nutritional content of food to individual health status, there are several considerations that can be informative and raise troubling concerns. For many decades, researchers have investigated the relationships between health status and consumption of extra virgin olive oil. Extra virgin olive oil (and oleic acid) is considered important for the prevention and coronary heart disease. While the biomolecular aspects involving G protein need further research, oleic acid levels in platelets may be a discriminating factor, together with linoleic and arachidonic acid, for coronary heart disease. There is still a huge debate regarding the effects of oleic acid alone or in combination with antioxidants.

Coronary Heart Disease (CHD) is the main cause of death and morbidity in industrialized countries. The incidence of myocardial infarction, however, is highly variable, with lower rates in Mediterranean countries compared to those in northern Europe, USA, or Australia [1]. Paradoxically, the low incidence of myocardial infarction occurs in spite of a high prevalence of classical cardiovascular risk factors [2].

Olive oil is the primary source of fat in the Mediterranean diet. The beneficial effects of olive oil on CHD have now been recognized, and are often attributed to the high levels of mono-unsaturated fatty acids (MUFA) [3]. Indeed, in November 2004, the US Federal Drug Administration (FDA) allowed a claim on olive oil labels concerning “the benefits on the risk of coronary heart disease of eating about two tablespoons (23 g) of olive oil daily, due to the MUFA in olive oil” [4].

2. A crucial element for a healthy heart: oleic acid and platelets

Oleic acid, and especially that obtained from pressing olives, is a crucial element in the prevention of ischemic cardiovascular disease, as has been demonstrated by a series of international scientific activity. Fatty acids other than n-3 Polyunsaturated Fatty Acids (PUFAs) can interact with the metabolism of eicosanoids and potentially influence platelet function. For example, there is evidence that diets rich in unsaturated fatty acids, such as linoleic acid and oleic acid, can also decrease thromboembolic risk by replacing arachidonic acid in platelet phospholipids, decreasing, at least in vitro, the production of thromboxane A₂ [TXA₂] and platelet aggregation. However, there is little conclusive evidence that platelet function in vivo is affected by diet [5].

Oleic acid has been found to be a potent inhibitor of platelet aggregating factor (PAF) and serotonin secretion. Consequently, in order to understand the molecular mechanisms of oleic acid action, the effects of this fatty acid on several biochemical events associated with platelet aggregation induced by PAF have been investigated. In particular, it has been found that oleic acid causes a decrease in the levels of phosphatidyl inositol phosphate (PIP) and PIP₂, which is associated with an inhibition of platelet aggregation induced by PAF. These results suggest that inhibition of the PAF response by oleic acid may be at least one of the steps involved in signal transduction [6].

Several literature reports have further suggested that olive oil may inhibit platelet function. This possible effect is of interest for two reasons. First, it may contribute to the apparent anti-atherogenic effects of olive oil, and second, it may invalidate the use of olive oil as an inert placebo in studies of platelet function. After exposure to olive oil, platelet aggregation and TXA₂ release decreased, and the content of platelet membrane oleic acid increased significantly; platelet membrane arachidonic acid content was found to significantly decrease. This suggests that excess of oleic acid impairs the incorporation of arachidonic acid into platelet phospholipids.

Olive oil also has an inhibitory effect on various aspects of platelet function, which might be associated with decreased risk for heart disease, although fish intake also plays a protective role [7].

The beneficial effects of olive oil can be attributed to its high content of oleic acid (70-80%). The consumption of olive oil increases the levels of oleic acid in cell membranes, which helps to regulate the structure of membrane lipids through the control of signal-mediated G-protein, causing a reduction in blood pressure [8].

In rats, cardiovascular tissues treated with 2-OHOA (hydroxy oleic acid) show activation of cAMP in response to activation of G_sα protein, which can be attributed to increased expression of G_sα proteins. As a result, there is significant reduction in systolic blood pressure [9]. The involvement of G_sα protein is also of interest considering the hypothesis forwarded by Cocchi, Tonello, Rasenick and Hameroff in psychiatric disorders as depression, suicide etc. (private meeting, 2008). In light of the below model, the role of G_sα protein in ischemic heart disease merits further investigation.

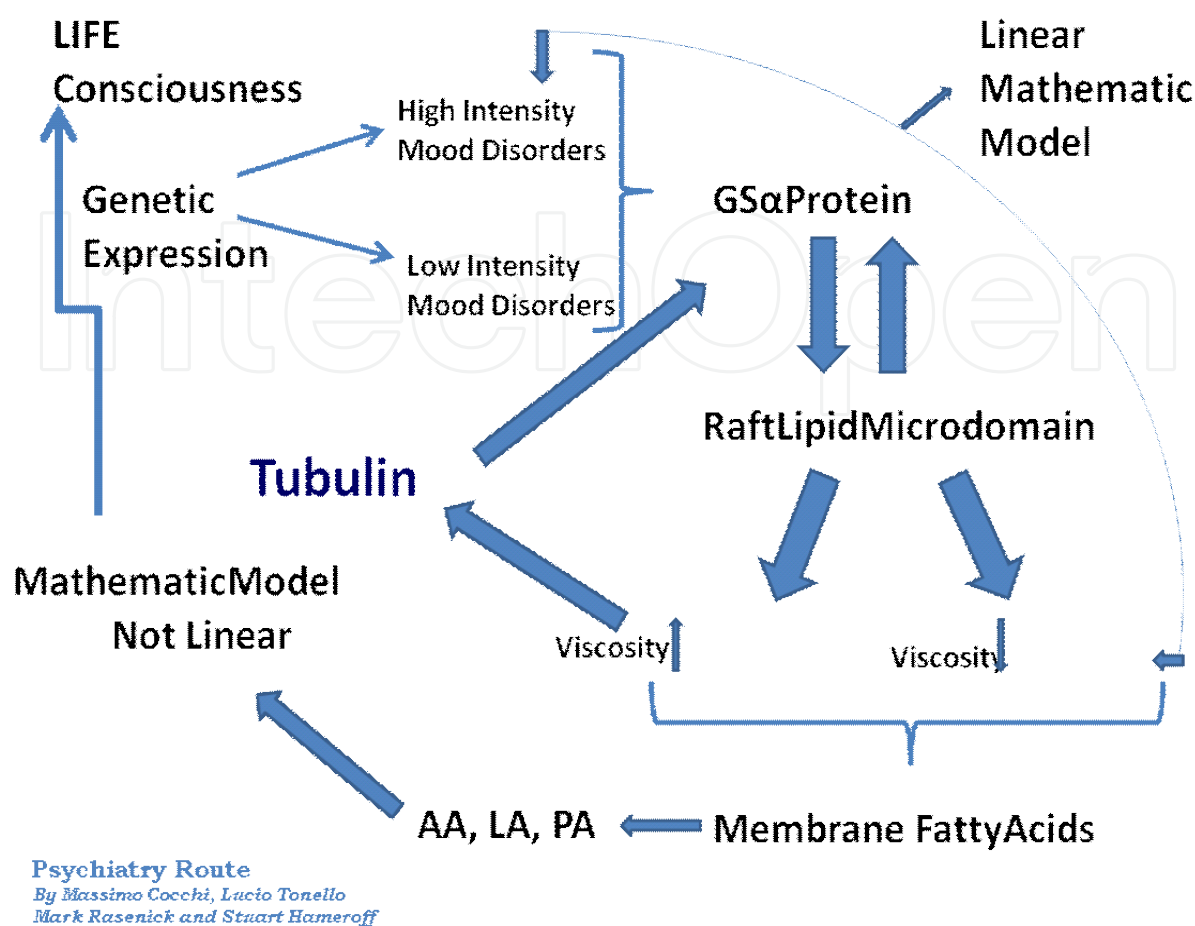


Figure 1. Description of selected biochemical and biomolecular events potentially involved in psychiatric disorders.

In figure 1, the molecular depression hypothesis described by Cocchi et al. [10], Donati et al. [11] and Hameroff and Penrose [12] is shown. Because of the possible similarity of the platelet to neurons, membrane viscosity can modify G α protein status. The G α protein is associated with tubulin. Depending on local membrane lipid composition, tubulin may serve as a positive or negative regulator of phosphatidylinositol bisphosphate hydrolysis (PIP₂) similar to G proteins. Tubulin is known to form high-affinity complexes with certain G proteins. The formation of these complexes allows tubulin to activate G α protein and creates a system whereby elements of the cytoskeleton can influence G-protein signaling. Rapid changes in membrane lipid composition or the cytoskeleton can modify neuronal signaling through such a mechanism.

Protein kinase C (PKC) activation (Figure 2) is preceded by a number of steps, originating from the binding of an extracellular ligand that activates a G-protein on the cytosolic side of the plasma membrane. This G-protein, using guanosine triphosphate (GTP) as an energy source, then activates protein kinase C (PKC) via the phosphatidylinositol bisphosphate (PIP₂) intermediate, which is shown as the diacylglycerol DAG/IP₃ complex. Several studies have shown that a reduced functionality of the serotonin (5-HT) transporter in some psychiatric disorders, such as obsessive-compulsive disorder (OCD), may be related to alterations

in its regulation at an intracellular level. PKC has also been reported to provoke a decrease in the number of 5-HT transporter proteins. The increased activity of PKC in OCD may be the result of increased activity of the phosphatidylinositol pathway.

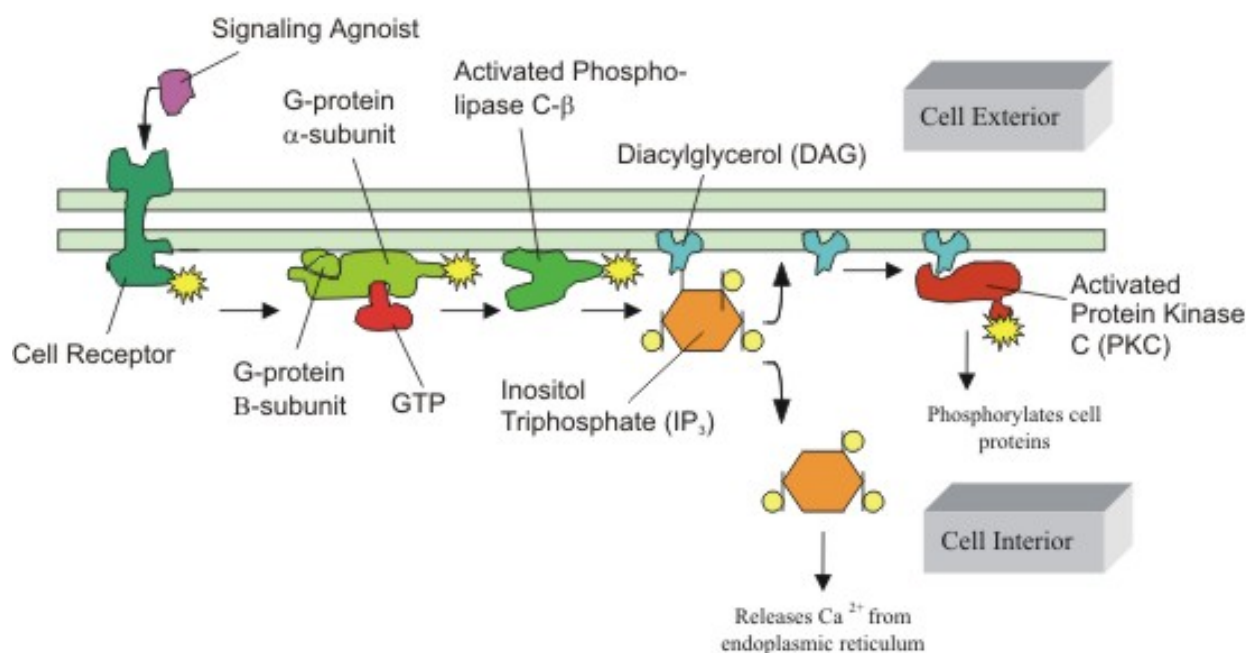


Figure 2. Description of PKC activation. Adapted from Alberts et al. [13].

The exclusive use of olive oil during food preparation seems to offer significant protection against ischemic heart disease, in spite of poor clinical conditions, lifestyle and other characteristics of individuals [14]. In addition, several historical papers have reported on the positive effects of olive oil on CHD.

In 1985, Mattson and Grundy [15] reported that olive oil reduces HDL cholesterol, which plays a protective, anti-atherogenic function, favoring the elimination of LDL-cholesterol. In 1986, Sirtori et al. [16] have shown that in addition to its effects on cholesterol and atherosclerosis, olive oil has preventive action on thrombosis and platelet aggregation. High intake of olive oil is not harmful, and reduces the levels of LDL-cholesterol, but not HDL [17 - 25].

3. Oleic acid and Atherogenesis

Atherosclerosis is considered to be an inflammatory disease [26], and endothelial dysfunction occurs early in the development of the pathology. Traditional risk factors for atherosclerosis promote endothelium activation, which induces adhesion and trans-endothelial migration of monocytes [26]. Several inflammatory mediators are released by the endothelium such as the eicosanoids derived from n-6 PUFA arachidonic acid. These include prostaglandin E₂ (PGE₂), leukotriene B₄, a chemoattractant and neutrophil activator, thromboxane, a potent vasoconstrictor, and platelet-aggregating factor [27].

Monocytes and macrophages are critical cells present in all stages of atherosclerosis. In addition to promoting LDL oxidation through free radical production, they also secrete proinflammatory cytokines such as IL-1 and Tumor Necrosis Factor (TNF), which stimulate the expression of adhesion molecules such as intercellular cell adhesion molecule-1 (ICAM-1), vascular-cell adhesion molecule-1 (VCAM-1), and E-selectin [25]. Circulating monocytes are attracted by these molecules and adhere to the endothelium, from which they transmigrate to the subendothelial space. Once within the endothelium, monocytes differentiate into macrophages, which in turn scavenge oxidized LDL, thus becoming foam cells and lead to plaque formation.

The proinflammatory response releases a principal messenger from macrophages, namely cytokine IL6. After engagement of its receptor on the liver, IL6 promotes the secretion of C Reactive Protein (CRP), a prototypic marker of inflammation [28, 29]. Serum IL6 and CRP have been shown to be predictive of CHD. Altered levels of serum CRP, IL6, and ICAM-1 have been associated with progression of atherosclerosis, and IL6 has been shown to be a good predictor of progressive peripheral atherosclerosis [30, 31].

The inflammatory protection of diets rich in oleic acid has been attributed to a decrease in the content of LDL linoleic acid [32]. The low susceptibility of oleic acid to oxidation, and the scavenging capacity of minor compounds in olive oil, can decrease the activation of proinflammatory transcription factors, such as nuclear factor-kappa B (NFkB), through a reduction of reactive oxygen species and peroxy radicals [33]. In this regard, it has been reported that consumption of meals enriched in olive oil do not activate NFkB in monocytes in contrast to meals rich in butter and walnut-enriched meals [34]. Studies on oleic acid enriched liposomes and vascular endothelium exposed to oleic acid, however, suggest a protective mechanism of oleic acid on free radical generation, oxidative damage to lipids, and inflammatory activity [35, 36].

Recent data suggest that oleic acid is not the only agent responsible for the anti-inflammatory properties of olive oil. In experimental studies, minor components of the unsaponifiable fraction of olive oil, such as alpha-tocopherol, beta-sitosterol, and triterpenes, in addition to phenolic compounds, have all been shown to have both anti-inflammatory and anti-endothelial activation properties [37]. The results of a meta-analysis of 14 studies carried out during 1983–1994 showed that the replacement of SFA by oils enriched in MUFA or PUFA had similar effects on total, LDL, and HDL cholesterol, whereas PUFA-enriched oil had a slight triglyceride-lowering effect [38]. Dubois et al. [39] showed that increasing the amount of fat up to 50 g led to stepwise increases in the postprandial rise of serum triglycerides, while the ingestion of 15 g fat had no effect on postprandial lipemia or lipoproteins in healthy adults. A meal containing 31 g of fat induced considerably less variations in lipemia, chylomicrons, and lipoproteins than a 42 g fat meal [39]. A single dose of 25 mL olive oil was not found to promote postprandial lipemia [40], in contrast to 40 mL and 50 mL doses [41, 42] with no effect on the phenolic content of the olive oil.

Abia et al. [43] reported that virgin olive oil intake resulted in lower postprandial triacylglyceride-rich-lipoprotein (TRL) levels and a faster disappearance of TRL-TG from blood, compared to intake of sunflower oil with a high content of oleic acid. Chylomicrons produced

after olive oil [44, 45] or n-3 PUFA [46] ingestion seem to enter the circulation more rapidly, and cleared at a faster rate, in comparison to those produced after intake of fats rich in SFA or PUFA. Although fat intake appears to be the major nutritional determinant of the postprandial triglyceride response, it is also influenced by other dietary components, including fiber, glucose, starch, and alcohol in a meal [47].

The oxidative modification of LDL plays a key role in development of atherosclerosis and CHD. Oxidation of lipids and lipoproteins present in LDL leads to a change in the lipoprotein conformation by which LDL are more facilitated to enter the monocyte/macrophage system of the arterial wall, and promote the atherosclerotic process [48]. It is currently believed that oxidized LDL are more damaging to the arterial wall than native LDL [49]. Elevated concentrations of circulating oxidized LDL show a positive relationship with the severity of acute coronary events [50, 51]. They are also independently associated with carotid intima-media thickness [52] and are predictors for CHD both in CHD patients [53] and the general population [54]. Several studies have been performed comparing the effects of MUFA-rich diets on the susceptibility of LDL to oxidation with those of PUFA- or carbohydrate-rich diets. Oleate-rich LDL have been shown to be less susceptible to oxidation than linoleate rich LDL [55-61].

4. Depression and Ischemic Heart Disease: a common role for oleic acid?

Because of the particular role of platelets on depressive and thrombogenic risk, our group has investigated the platelet fatty acid profile in three groups of subjects: healthy (n=60), ischemic (n= 50) and depressive (n= 84). The aim of the study was to understand which fatty acid could be utilized as markers of ischemic cardiovascular pathology and depressive disorder, and to classify subjects using an artificial neural network (ANN). All the ANNs tested gave essentially the same result. However, one type of ANN, known as Self-Organizing Map (SOM), [62, 63, 64], gave additional information by allowing the results to be described in a two-dimensional plane with potentially informative border areas. The central property of the SOM is that it forms a nonlinear projection of a high-dimensional data manifold on a regular, low-dimensional (usually 2D) grid.

A series of repeated and independent SOM simulations, with the input parameters being changed each time, led to the finding that the best discriminating map was that obtained by inclusion of the following three fatty acids: palmitic acid (C16:0), linoleic acid (C18:2 *n*-6) and arachidonic acid (C20:4 *n*-6) for depressive subjects and oleic acid (C18:1), linoleic acid and arachidonic acid for ischemic subjects [10, 65-67] (Figures 3, 4).

5. A case study

A 42-year-old female with a very high familial risk for ischemic cardiovascular disease (one sister 34 years old died of heart attack; another sister, 48 years old, heart attack; uncle, two infarctions; mother, 69 years old, died of heart attack; aunt, 59 years old, died of heart at-

tack), was submitted to a classic complete functional cardiovascular investigation which resulted negative. The subject is a heavy smoker, cholesterol: 230 mg/dl, HDL: 84 mg/dl. Framingham score: 13 (low risk score). Platelet levels of oleic acid, linoleic acid and arachidonic acid were analyzed using the SOM designed for ischemic patients, and the concentrations of those fatty acids were entered in the SOM. The subject detailed information on the study and provided informed consent. The patient's fatty acid triplet, tested in the SOM, gave the following result (Figure 5).

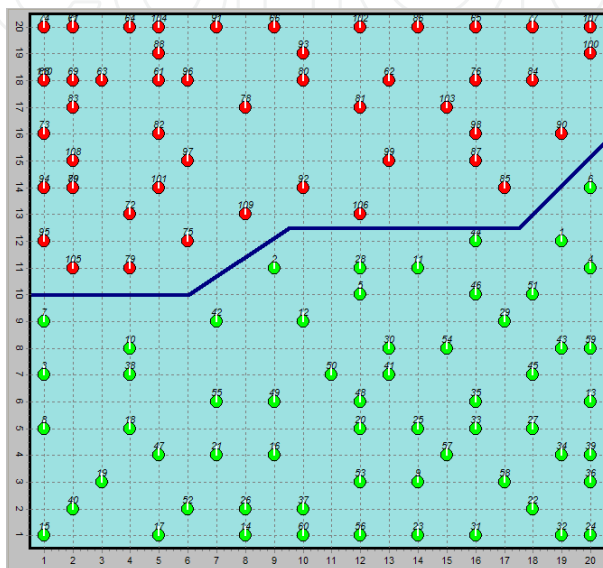


Figure 3. SOM classification of depressive subjects (red) against normal subjects (green). Platelet arachidonic acid ($C_{20:4}$), palmitic acid ($C_{16:0}$), and linoleic acid ($C_{18:2}$) can discriminate depression and have diagnostic power.

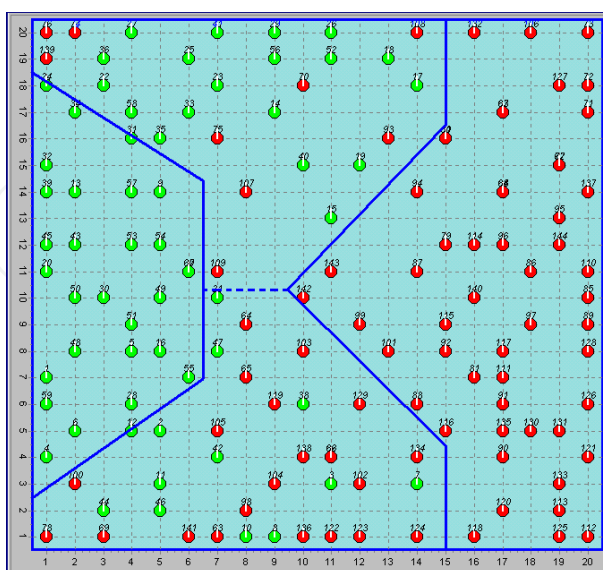


Figure 4. SOM classification of ischemic subjects (red) against normal subjects (green). Platelet oleic acid ($C_{18:1}$), arachidonic acid ($C_{20:4}$), linoleic acid ($C_{18:2}$) can discriminate ischemia and have diagnostic power.

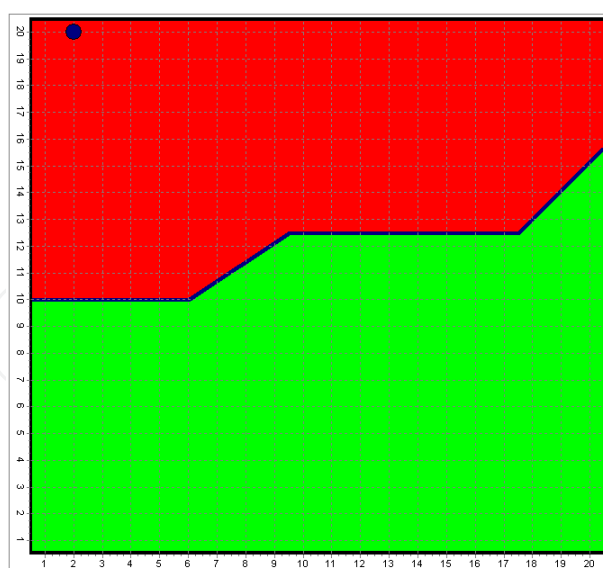


Figure 5. Position of the patient according to the three fatty acids (oleic, linoleic and arachidonic) on the SOM, which classifies ischemic patients.

This result was compared with the SOM classification of normal and pathologic subjects, as shown in figure 4. The patient was asked to submit herself to a Coronary TAC and the images showed "Interventricular Anterior (IVA) branch: small mixed plaque in the proximal tract, 33% of the lumen" (radiological diagnosis). The result suggests the opportunity to select young high risk subjects to evaluate not only the diagnostic power of the SOM, but also the possibility for early diagnosis of plaque formation. A large trial is necessary to validate this result, but based on the classical rules of Evidence Based Medicine, it is very difficult to obtain approval from an ethic's committee.

Medical science has not yet fully understood or accepted the use of the ANN mathematic models in relation to experimental conditions, which are still strongly linked to traditional protocols. The task of finding biomarkers according to the rules dictated by Evidence Based Medicine requires the elimination of selection bias, and leads to selection of a population that may be clinically unrealistic. The characteristics of the above-described method nonetheless allow the analysis to be carried out, and permit to find differences among subsets of the population.

The first fundamental consequence of the use of fatty acids is that an extremely effective and practical diagnostic tool can be obtained, with a strong tolerance to "noise". Secondly, the choice of specific fatty acids and their relative strength in the classification by the SOM allows investigating more in-depth investigation of the problem and helps in understanding the disease from the biochemical point of view.

6. Commonalities between CHD and depression

To demonstrate the powerful grouping capacity of the SOM, we created a new network where all three groups were inserted and grouped simultaneously on the basis of the char-

acteristics of the triplets previously highlighted, which were all different from one another [68] (Figure 6).

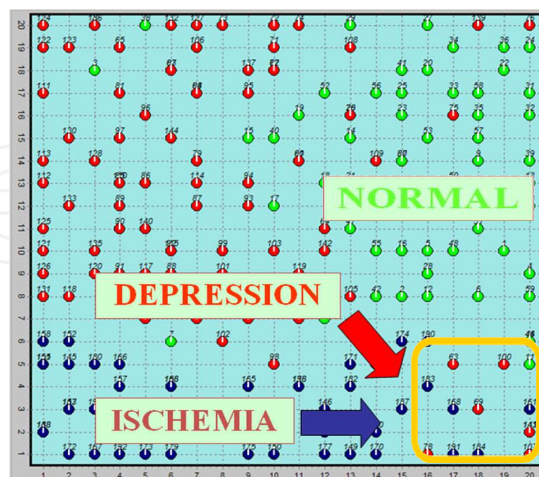


Figure 6. Simultaneous classification, using the SOM, of three groups of subjects (normal, depressive and ischemic). In the right corner of the map, ischemic and depressive subjects are mixed and have, in common, a low level of platelet oleic acid.

As shown by the SOM, it is possible that reduced amounts of oleic acid not only are critical in the biochemical classification of ischemic heart disease, but are also common to a condition that characterizes a relationship between depression and ischemia [69]. It seems possible that levels of C18:1 in platelets dominate in ischemia, and are linked to depression. Furthermore, it can be conjectured that there are two different types of depression, namely classical and ischemia-induced according to the findings of different platelet membrane viscosity and its effect at the biomolecular level. [10-12, 70]. The relationships between depression and ischemic heart disease have been widely studied [71, 72]. Interestingly, Weyers and Colquhoun [73] reported improvements in depressive symptoms in patients with CHD after consumption of olive oil.

7. Do we eat enough extra virgin olive oil?

The question then arises as to whether there is sufficient consumption of olive oil and oleic acid in the Italian population. Knowing that oleic acid can significantly change the composition of platelet fatty acids, which are crucial in the genesis of plaque formation, and can significantly alter the amount of oleic acid in platelet membranes, an experiment on a large group of pigs (80 Duroc x Large White) was performed [74]. Four groups of pigs were studied, 20 animals each, which received four diets containing different lipid fractions, as follows:

Diet 1: corn oil (low linoleic acid.), diet 2: corn oil (medium linoleic acid.), diet 3: sunflower oil (high oleic acid.), diet 4: sunflower oil (high oleic acid) + palm oil (high palmitic acid). The diets fed to animals, to meet the needs for growth, had the following lipid composition (Table 1):

Period (kg)	Diet	EE	C16:0	C18:0	C18:1n9	C18:2n6	C18:3n3
50 - 90	1	2.70	13.13	2.05	31.07	50.90	2.59
50 - 90	2	2.86	14.37	2.04	26.40	54.54	2.42
50 - 90	3	5.30	8.91	2.39	56.47	30.23	1.27
50 - 90	4	5.37	18.67	8.36	39.99	30.86	1.40
90 - 120	1	2.63	12.83	1.72	31.60	51.15	2.38
90 - 120	2	2.57	14.16	1.94	25.76	54.96	2.55
90 - 120	3	5.56	8.81	2.44	57.12	29.73	1.26
90 - 120	4	5.62	20.02	9.26	39.41	29.59	1.12
120 - 160	1	2.83	13.32	1.69	30.46	52.00	2.41
120 - 160	2	2.89	13.75	1.88	25.65	56.29	2.35
120 - 160	3	5.74	8.54	2.10	57.18	30.91	1.07
120 - 160	4	5.76	19.71	9.25	39.16	30.25	1.17

Table 1. Ether extract (% dry Matter) and fatty acid composition of lipid fractions

Fatty Acids		C16:0	C18:0	C18:1n9	C18:2n6	C18:3n3	C20:4
Diet 1	Media s.d.	28.51 ^a	32.00	17.38 ^B	9.30	0.63a	12.19 ^{AB}
		1.84	10.70	5.63	3.40	0.36	5.18
Diet 2	Media s.d.	27.73 ^{ab}	29.01	18.0 ^B	9.07	0.48ab	15.6 ^A
		1.47	8.48	3.17	2.88	0.29	4.52
Diet 3	Media s.d.	27.00 ^{ab}	27.78	24.93 ^A	9.37	0.34 ^b	10.59 ^B
		2.07	8.12	6.78	3.10	0.25	4.48
Diet 4	Media s.d.	26.51 ^b	32.04	19.36 ^B	9.32	0.51 ^{ab}	12.25 ^{AB}
		2.63	11.07	5.43	3.64	0.32	4.27
P		<0.05	n.s.	<0.01	n.s.	<0.05	<0.01

Table 2. Mean values ± SD of platelet fatty acids in the different treatment groups

The platelet fatty acids (Table 2) were plotted as for ischemic and normal human subjects in the SOM for ischemia (Figure 7).

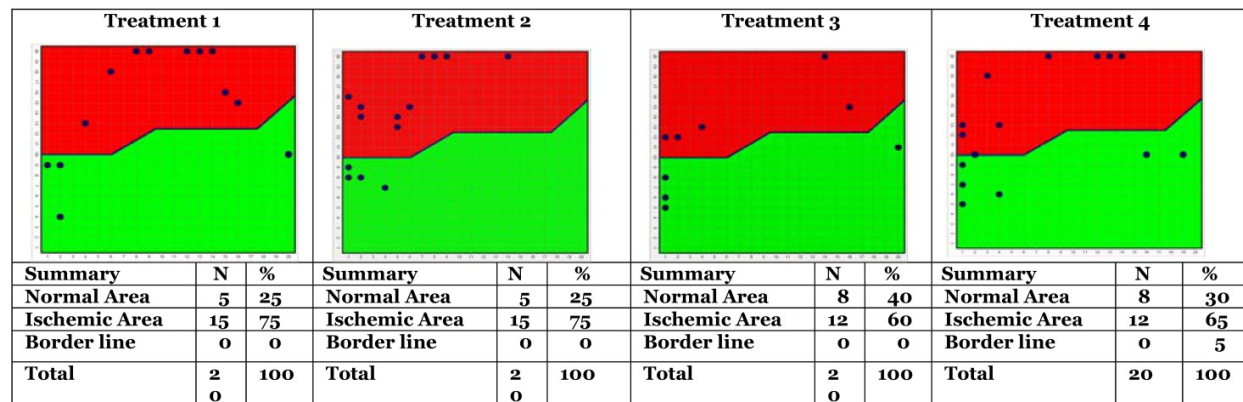


Figure 7. By increasing the oleic acid content in diets is possible to move pig platelets, in agreement with the fatty acid triplet [66, 67], from the pathologic (red area) to the normal (green area) area.

It is feasible to obtain similar results in humans. If one considers the characteristics described for the pig model of atherosclerosis [75], and applying similar characteristics to humans, it can be assumed that we should consume a quantity of oleic acid, and consequently, extra virgin olive oil, that is at least twice that of current levels. To demonstrate this, we made simple considerations based on the purchase of olive oil in Italy (Data provided by the Istituto di Servizi per il Mercato Agricolo Alimentare (ISMEA)).

Based on data provided and taking into account that the value derived from the table should be increased by 40%, since about 40% of purchase data were excluded, the consumption of extra virgin olive oil for each Italian is on average, about 11.76 grams of oleic acid daily, considering that olive oil is on average value about 70% oleic acid. This value is even likely to be less, as much oil is also used for frying, and therefore cannot be included as part of raw consumption. While this quantity is very small, there are also regional differences between the north and south of Italy.

This observation is also related to the observation that current eating behavior does not allow large consumption of olive oil. It should be remembered that meals eaten out of the household, often consisting of a sandwich, make it difficult to consume extra virgin olive oil in larger quantities. While the eating habits of rural areas may still be able to compensate this situation, there is an increasing trend to gradually move away from such traditions.

Recently, we investigated the consumption of olive oil in a restaurant in the Center-North of Italy, (2750 subjects in one month). The average consumption of olive oil was 1.8 g per customer per month, which corresponds to about 1.26 g of oleic acid. Together with the above cited data, this results confirms that olive oil is not consumed in large quantities. Given this, as Ancel Keys pointed out, one wonders if the Mediterranean diet is still a model of health, considering the consumption of extra virgin olive oil.

Systematic name	Trivial name	Shorthand designation	Molecular weight	Melting point (°C)
butanoic	butyric	4:0	88.1	-7.9
pentanoic	valeric	5:0	102.1	-19
hexanoic	caproic	6:0	116.1	-3.4
octanoic	caprylic	8:0	144.2	16.7
nonanoic	pelargonic	9:0	158.2	12.5
decanoic	capric	10:0	172.3	31.6
dodecanoic	lauric	12:0	200.3	44.2
tetradecanoic	myristic	14:0	228.4	53.9
hexadecanoic	palmitic	16:0	256.4	63.1
heptadecanoic	margaric (daturic)	17:0	270.4	61.3
octadecanoic	stearic	18:0	284.4	69.6
eicosanoic	arachidic	20:0	312.5	75.3
docosanoic	behenic	22:0	340.5	79.9
tetracosanoic	lignoceric	24:0	368.6	84.2
<i>cis</i> -9-hexadecenoic	palmitoleic	16:1(n-7)	254.4	0.5
<i>cis</i> -9-octadecenoic	oleic	18:1(n-9)	282.4	16.2
<i>trans</i> -9-octadecenoic	elaidic	tr18:1(n-9)	282.4	43.7
<i>cis</i> -11-octadecenoic	<i>cis</i> -vaccenic (asclepic)	18:1(n-7)	282.4	39
<i>cis</i> -9-eicosenoic	gadoleic	20:1(n-11)	310.5	25
<i>cis</i> -13-docosenoic	erucic	22:1(n-9)	338.6	33.4
9,12-octadecadienoic	linoleic	18:2(n-6)	280.4	-5
6,9,12-octadecatrienoic	γ-linolenic	18:3(n-6)	278.4	
9,12,15-octadecatrienoic	α-linolenic	18:3(n-3)	278.4	-11
8,11,14-eicosatrienoic	dihomo-γ-linolenic	20:3(n-6)	306.5	
5,8,11,14-eicosatetraenoic	arachidonic	20:4(n-6)	304.	-50
6,9,12,15-octadecatetraenoic	stearidonic	18:4(n-3)	276.4	-57
5,8,11,14,17-eicosapentaenoic	EPA	20:5(n-3)	302.5	-54
7,10,13,16,19-docosapentaenoi	DPA	22:5(n-3)	330.6	
4,7,10,13,16,19-docosahexaenoic	DHA	22:6(n-3)	328.6	-44

(see: http://216.239.59.104/search?q=cache:qTHq_xfePkIJ:www.cyberlipid.org/fa/acid0001.htm+Aitzetm%C3%BCller+K&hl=it)

Table 3. Selected chemical and physical characteristics of fatty acids

8. Chemical and technological considerations about oleic acid

Fatty acids have different functions in living organisms, including the structural one, which are determined by the length of their hydrocarbon chain and the presence or absence of double bonds. Hydrocarbon chain length, in the same conditions of unsaturation, is directly proportional to the melting point (as well as the boiling point) (Table 3). The solubility in water (Table 4) and unsaturation, for the same chain length, is inversely proportional to the melting point (see Table 3), with very few exceptions.

Carbon number	Solubility
2	Infinite
4	Infinite
6	9.7
8	0.7
10	0.15
12	0.055
14	0.02
16	0.007
18	0.003

Table 4. Fatty acid solubility in water at 20°C (in grams per liter)

These chemical differences are determined in large part by chemical and physical interactions that exist when molecules are close enough to unsaturate them. In the case of fatty acids, the possibility to join molecules depends only on the hydrocarbon chain (Van der Waals forces), which is facilitated when it is saturated and more difficult when unsaturated (especially at the point of unsaturation). The longer and more linear the chain, the greater the interaction, and the more unsaturated it will be, consequently, the interaction will be lower. When fatty acids are part of a triglyceride or phospholipid, the effect occurs in a similar manner and therefore, in biological membranes, a greater or lesser chance of interaction corresponds to greater or lesser "fluidity" of the membrane, which is proportional to more or less functionality (permeability).

At room temperature, in terms of membrane structure, fatty acids are important, and the ones that are more widespread in nature are those with 18 total carbon atoms, especially unsaturated. Modulation of proper membrane fluidity requires that some fatty acids are relatively "rigid", such as palmitic and stearic acid, with a preference for the former since it has a lower melting point and thus is more effective in bringing about small changes.

One of the most important aspects of biological systems that protect themselves through membranes is the preservation of integrity of the membrane itself, which is subject to con-

tact with chemical reactive oxygen species (ROS), and capable of chemically attacking the unsaturated zone of the molecule. Greater effectiveness is related to a greater level of unsaturation, leading to subsequent breakage of the molecule with increased membrane fragility. For these reasons, the membrane is associated with a series of antioxidants, whose action is linked to their position in the membrane [75]. Oleic acid is the least oxidizable among unsaturated fatty acids (Table 5), and is also not too fluid or too rigid, and is thus suitable for prolonging membrane stability [76, 77].

FATTY ACID	1) AUTOXIDATION	2) AUTOXIDATION	PHOTOSENSITIZED OXIDATION (PHOTOXIDATION)
SATURATED	1	1	
MONOENES	10	100	1.1 (32,000)*
DIENES	100	1200	2.9 (1600)*
TRIENES	200	2500	3.5
TETRAENES**	300		
PENTAENES**	400		
HESAENES**	500		

* In brackets ratio between photooxidation and autooxidation is shown

** Hypothesis based on physical-chemical behavior

Table 5. Oxidation rate of several unsaturated fatty acids [Modified from Gunstone et al. [76]]

The rate of oxidation between various unsaturated fatty acids shown in Table 5 appears increased between oleic acid (monoenes) and linoleic acid (dienes), but upon increasing the unsaturation (trienes), the variation is much less pronounced. In biological systems, the position of the fatty acid in glycerides or phospholipids [77] appears to influence the rate of oxidation, and is slower when inserted in position 2, or in the β position of the molecule. In the case of olive oil, as in all vegetable fats (Table 6), the 2 position is occupied by unsaturated fatty acids, and is more available in that position because it can directly cross the intestinal wall of the 2-monoglycerides, resulting from digestion of glycerides by pancreatic lipase. In particular, on a molar basis, 83% of unsaturated fatty acids, in position 2 of triglycerides in olive oil, is occupied by oleic acid.

For extra virgin olive oil, its total unsaturation makes it particularly stable (Table 7) [79, 80] so that appropriate conservation, which is further prolonged by the presence of numerous and effective natural antioxidants (biophenol), is still present after refining, in contrast to other oils.

Fat or Oil source	Fatty acid position	14:0	16:0	18:0	18:1	18:2	18:3	20:0	22:0
Women milk*	1	3.2	16.1	15.0	46.1	11	0.4		
	2	7.3	58.2	3.3	12.7	7.3	0.6		
	3	7.1	6.2	2.0	49.7	2.0	1.6		
Women milk	1	18.2	20.0	73.9	42.5	33.3	15.4		
	2	41.5	72.3	16.3	11.7	22.1	23.1		
	3	40.3	7.7	9.9	45.8	44.5	61.5		
Cow milk	1	11	36	15	21	1			
	2	20	33	6	14	3			
	3	7	10	4	15	<1			
Pig	1	1	10	30	51	6			
	2	4	72	2	13	3			
	3			7	73	8			
Cow	1	4	41	17	20	4	1		
	2	9	17	9	41	5	1		
	3	1	22	24	37	5	1		
Cocoa butter	1		34	50	12	1			
	2		2	2	87	9			
	3		37	53	9				
Groundnut	1		14	5	59	18		1	-
	2		1	<1	58	39		-	-
	3		11	5	57	10		4	6
Corn	1		18	3	27	50	1		
	2		2	<1	26	70	<1		
	3		13	3	31	51	1		
Soya	1		14	6	23	48	9		
	2		1	1	21	70	7		
	3		13	6	28	45	8		
Olive	1		13	3	72	10	<1		
	2		1	-	83	14	1		
	3		7	4	74	5	1		

Mol % = molar percentage

*Relative GC area % (<http://www.cyberlipid.org/index.htm>); ** Sørensen A.D.M. et al., 2010 [78]

Table 6. Main fatty acid (mol %) distribution in the three positions of glycerine molecule of the corresponding triacylglycerols (triglycerides) of several fats and oils.

Fattyacids											Total	
	Caprylic (C8:0)	Capric (C10:0)	Lauric (C12:0)	Mirystic (C14:0)	Palmitic (C16:0)	Stearic (C18:0)	Oleic (C18:1)	Linoleic (C18:2)	Linolenic (C18:3)	Eicosenoic (C20:1)	Unsaturat ^a (unstability factor)	Iodine number
Oil from:												
Groundnut				ND-0.1	8.0-14.0	1.0-4.5	35.0-69.0	12.0-43.0	0-0.3	0.7-1.7	200-481	86-107
Rapeseed (0 erucic)				ND-0.2	2.5-7.0	0.8-3.0	51.0-70.0	15.0-30.0	5.0-14.0	0.1-4.3	320-630	105-126
Safflower				ND-0.2	5.3-8.0	1.9-2.9	8.4-21.3	67.8-83.2	ND-0.1	0.1-0.3	700-740	136-148
Safflower (HO)				ND-0.2	3.6-6.0	1.5-2.4	70.0-83.7	9.0-19.9	ND-0.2	0.1-0.5	175-270	80-100
Sunflower			ND-0.1	ND-0.2	5.0-7.6	2.7-6.5	14.0-39.4	48.3-74.0	0-0.3	0-0.3	531-766	118-141
Sunflower (HO)				ND-0.1	2.6-5.0	2.9-6.2	70.0-90.7	2.1-20.0	ND-3.0	0.1-0.5	118-270	78-90
Corn			ND-0.3	ND-0.3	8.6-14.0	ND-3.3	20.0-42.0	34.0-65.6	0-1.2	0.2-0.6	400-481	103-135
Olive (CODEX)					7.5-20.0		55.0-83.0	3.5-21.0	Max 1.0	Max 0.4	163-285	75-94
Soya Bean			ND-0.1	ND-0.2	8.0-13.5	2.5-5.4	17.0-30.0	48.0-59.0	4.5-11.0	0-0.5	600-840	124-139
Grape seed				ND-0.3	5.5-11.0	3.0-6.5	12.0-28.0	58.0-78.0	0-1.0	0-0.3	596-802	128-150
Fat from:												
Cocoa butter					22.6-30.4	30.2-36.0	29.2-36.4	1.3-4.0	ND-0.5		370-380	34-40
Coconut	4.6-10	5.0-8.0	45.1-53.2	16.8-21.0	7.5-10.2	2.0-4.0	5.0-10.0	1.0-2.5	ND-0.2	ND-0.2	24-34	6.3-10.6
Palm			ND-0.5	0.5-2.0	39.3-47.5	3.5-6.0	36.3-44.0	9.0-12.0	ND-0.5	ND-0.4	130-391	50.0-55.0
<i>Palm olein</i>			0.1-0.5	0.5-1.5	38.0-43.5	3.5-5.0	39.8-46.0	10.0-13.5	ND-0.6	ND-0.4	158-187	56
<i>Palm stearin</i>			0.1-0.5	1.0-2.0	48.0-74.0	3.9-6.0	15.5-36.0	3.0-10.0	ND-0.5	ND-0.4	76-270	33
<i>Palm kernel</i>	2.4-6.2	2.6-5.0	45.0-55.0	14.0-18.0	6.5-10.0	1.0-3.0	12.0-19.0	1.0-3.5	ND-0.2	ND-0.2	33-51	14.1-21.0

^a Total unsaturation is calculated as the relative percentage of single fatty acid for a different factor, for each unsaturation, the degree is proportional to the oxidative instability. The factors utilized were: 1 for monounsaturated, 10 for diunsaturated and 20 for triunsaturated fatty acids. HO =high oleic. ND = not detectable

Table 7. Main fatty acid composition of fats and oils

Not all olive oils have the same concentration of oleic acid. The International Olive Oil Council (IOOC) has dictated that the content of oleic acid in olive oils can vary from 55% to 83% of total fatty acids [81]. The regulations of the European Community do not indicate the amount of oleic acid in olive oil, but simply indicate the specifications of several other parameters that are useful for detecting fraud and require the distinction between various commercial products obtained from olive processing.

Among these, extra virgin oils are those that must have the highest quality. Extra virgin olive oils with the highest content of oleic acid have always been regarded as those with the highest quality, but only because of their higher stability during storage, as a consequence of the low reactivity of oleic acid compared with polyunsaturated fats. The Food and Drug Ad-

ministration (FDA) has stated (November 1, 2004) that U.S. consumption of 23 g of olive oil each day (about two tablespoons) helps in prevention of cardiovascular diseases [4].

Today, there are other sources of oil high in oleic acid, such as safflower, sunflower and canola (the new name for rapeseed oil low in erucic acid), and therefore based solely on the content of oleic acid, these sources would also be optimal in this regard. However, the reputation of olive oil as a healthy product is most likely due to the presence of the numerous "minor elements" contained within [82, 83]. Among these minor components, several compounds are worthy of mention including biophenols, which consists of phenols and polyphenols with high antioxidant and antiradical activity, some triterpene alcohols, phytosterols, squalene, and tocopherols. These latter are considered important because of the content of vitamin E, and for their ability to facilitate the assimilation of polyunsaturated fatty acids: 1 mg allows the assimilation of 1 g of polyunsaturated fatty acids [84].

The discovery of health effects from the minor components in olive oil has led to a large gap in the nutritional properties of edible oils. In fact, oils from seeds, subject to refining, lose many minor components and do not have the health properties that the corresponding matrix has. The technology for olive processing influences the quality and organoleptic characteristics of the final product, which is not always considered by industrial operators as much of the scientific knowledge is particularly new. The olive oil is encapsulated in small drops (10-30 micrometers) within vacuoles with a polysaccharide wall: oil droplets, during processing, are released in crushing and come into contact with the other components of olives during grinding of the paste. It is the prolonged contact with the oil-pasta that allows joining of small droplets such that they can then leave the dough during the separation process that emulsifies all the minor components in oil.

Therefore, time and temperature of processing can also affect the final product, and even if the starting characteristics of the olives are similar they can yield very different products. Moreover, during the same oil-paste stage, enzyme activities are capable of forming the fragrance of the oil through a series of biochemical steps that, in part, may reduce the antioxidant ability of biophenol components and their effects on health. Therefore, choices made during the processing of olives should take these effects into consideration.

There are several hundred olive cultivars grown in Italy, which can produce many oils that have a very different composition, although all can be considered of excellent quality. In particular, the richness in antioxidants (especially biophenols) can affect characteristics of the oil in terms of taste, storage stability, and health properties. Even if much scientific knowledge has been learned about olive production and processing technology, there are still many questions that must be answered in order to improve the quality, especially those related to health, of the oils obtained by processing olives

9. Conclusion

The ability to transform, by the action of delta9-desaturase, stearic acid to oleic acid, and vice versa makes oleic acid very useful for the modulation of the fluidity (and functionality)

of cell membranes. Recalling that the fatty acid composition of platelets can be correlated with depression and also with ischemia [85], we can consider the oil obtained from olive processing such as the lipid substrate better balanced with respect to the fatty acid unsaturations, for the platelet membrane composition of normal individuals.

We must remember that the presence of high concentrations of oleic acid from olive oil is one of the stabilizing factors against oxidative modification, in both cases, for the oil itself and for cell membranes. Furthermore, the oil from olives when is classified as extra virgin, possesses a wealth of biophenols, powerful antioxidants predominantly of antiradical type, which further increase the stability of the oil and, more or less directly, even of the membrane lipids.

Olive oil, and, particularly an extra virgin olive oil-rich diet, decreases prothrombotic activity, and modify platelet adhesion, coagulation, and fibrinolysis. The wide range of antiatherogenic effects associated with olive oil consumption can help to justify the low rate of cardiovascular mortality found in southern European Mediterranean countries, in comparison with other western countries, despite a high prevalence of CHD risk factors. Experimental evidence confirms a critical role of reduced levels of oleic acid in platelets in ischemic subjects with a diagnostic discriminant capacity from normal subjects [85]. At present, although traditional cardiovascular risk factors are under revision, a new field of research in platelets, and in particular oleic acid and its relationship with linoleic and arachidonic acid, should be pursued. The mechanisms by which olive oil exerts its beneficial effects merit further investigation, and additional studies are required to document the benefits of olive oil consumption on primary endpoints for cardiovascular disease. In this regard, consumption of extra virgin olive oil and daily intake of oleic acid should, however, be promoted.

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