



# ALZHEIMER'S PREVENTION: NEW FRONTIERS



28 APRIL 2026 • ONLINE



## Why Phospholipids are a Brain Essential

Dr Simon Dyall

[Simon.Dyall@roehampton.ac.uk](mailto:Simon.Dyall@roehampton.ac.uk)

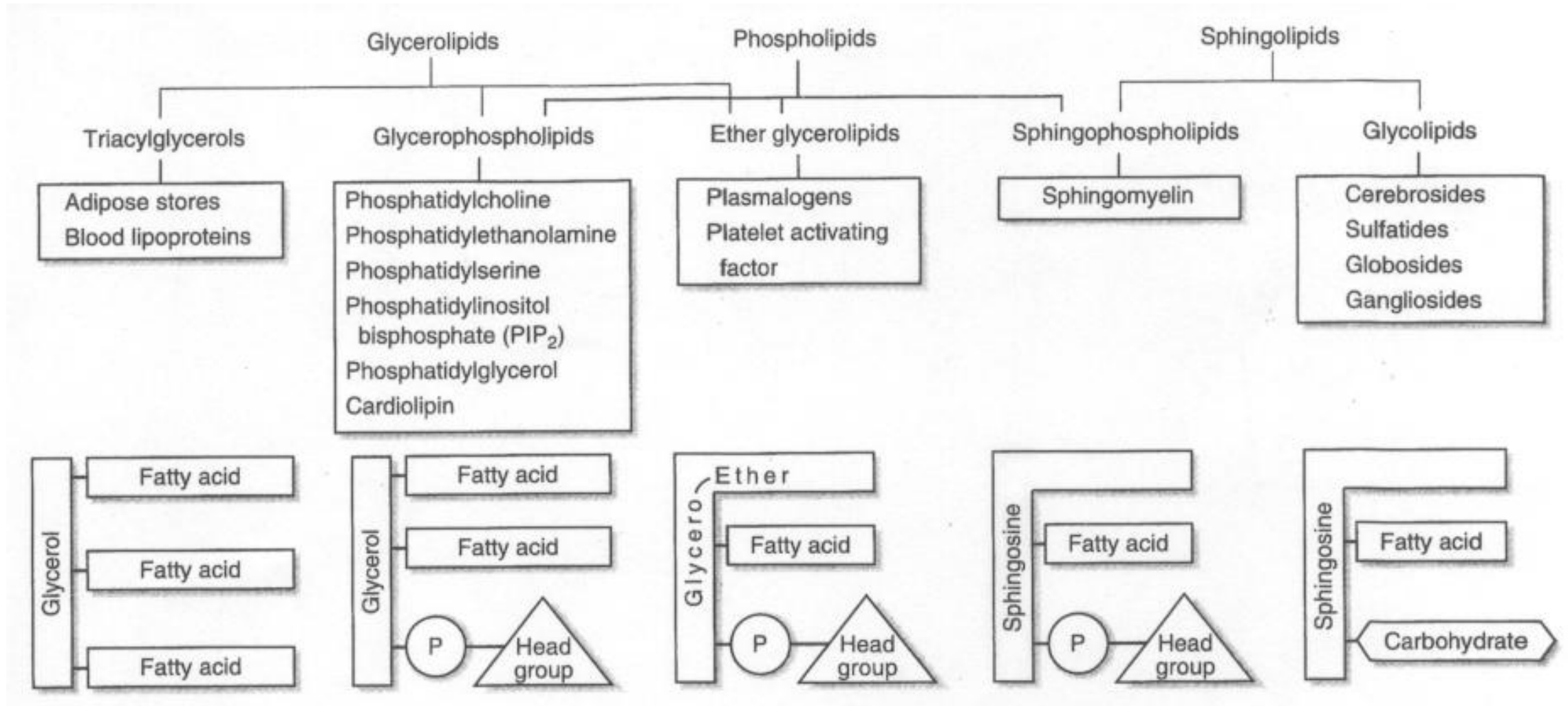


# Topics

- 1. What are phospholipids (PLs)?***
- 2. What do PLs do?***
  - Structure (bilayers in membranes)
  - Communication and reservoir of polyunsaturated fatty acids
- 3. Do PL levels change?***
- 4. How are PLs made and can they be increased?***

# ***1. What Are Phospholipids (PLs)?***

# Classes of Complex Lipids

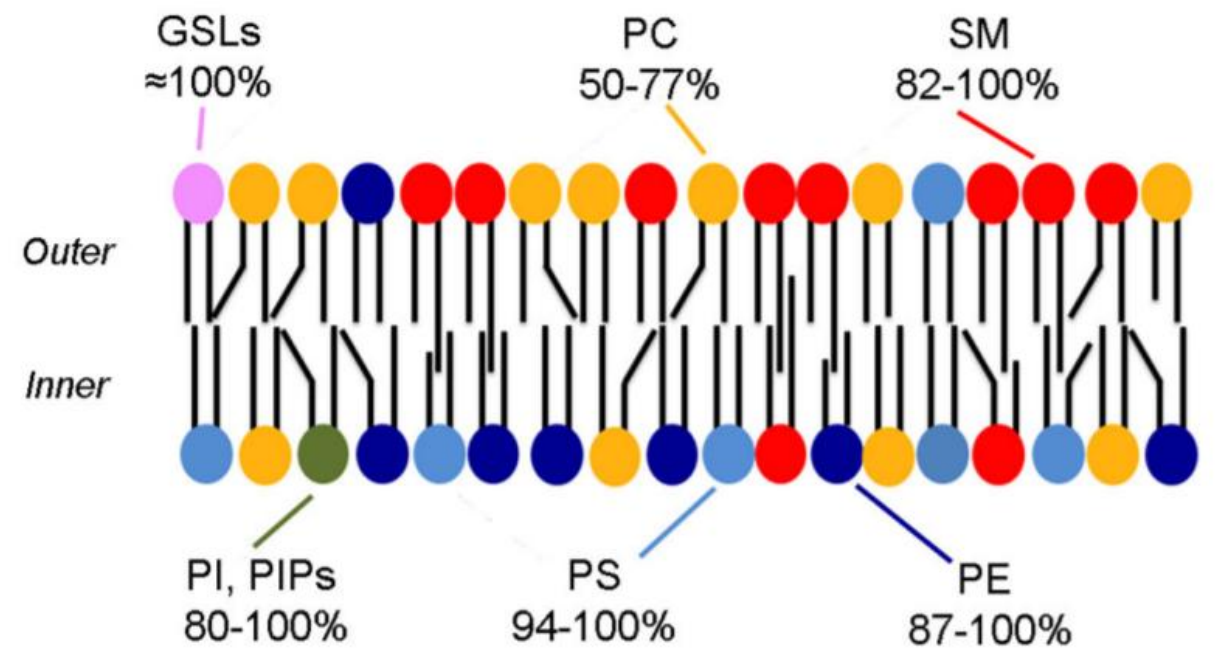


**Table 1:** Lipid composition of a typical nucleated mammalian cell

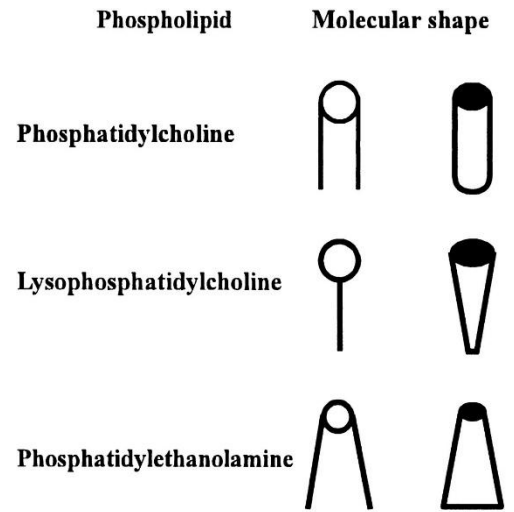
	Percentage of total lipids <sup>a</sup>
Phosphatidylcholine	45–55
Phosphatidylethanolamine	15–25
Phosphatidylinositol	10–15
Phosphatidylserine	5–10
Phosphatidic acid	1–2
Sphingomyelin	5–10
Cardiolipin	2–5
Phosphatidylglycerol	<1
Glycosphingolipids	2–5
Cholesterol	10–20

<sup>a</sup>Data are averaged from several sources.

(Vane 2014)



(Fulimoto and Parmryd 2017)



(Escribá *et al.*, 1997)

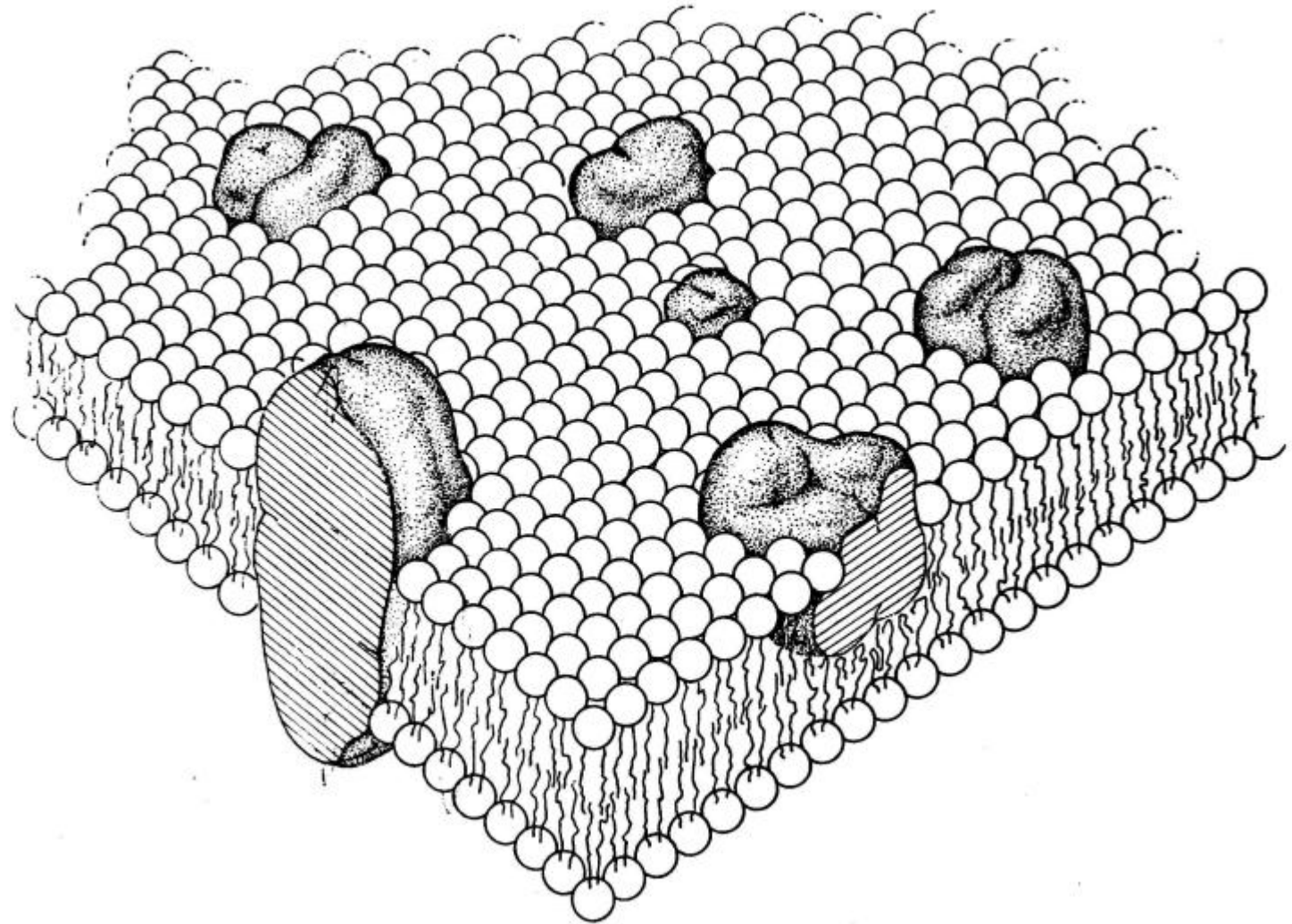
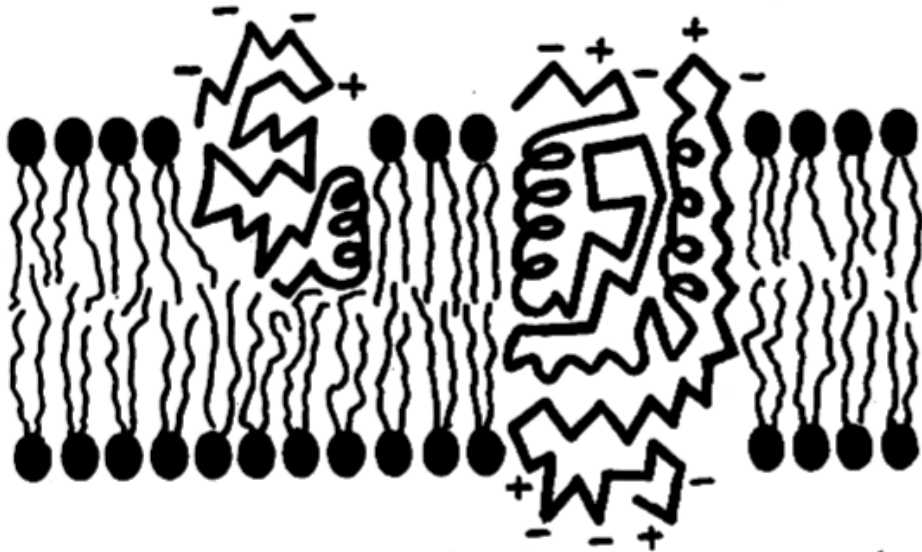
## ***2. What Do PLS Do?***

# The Fluid Mosaic Model of the Structure of Cell Membranes

Cell membranes are viewed as two-dimensional solutions of oriented globular proteins and lipids.

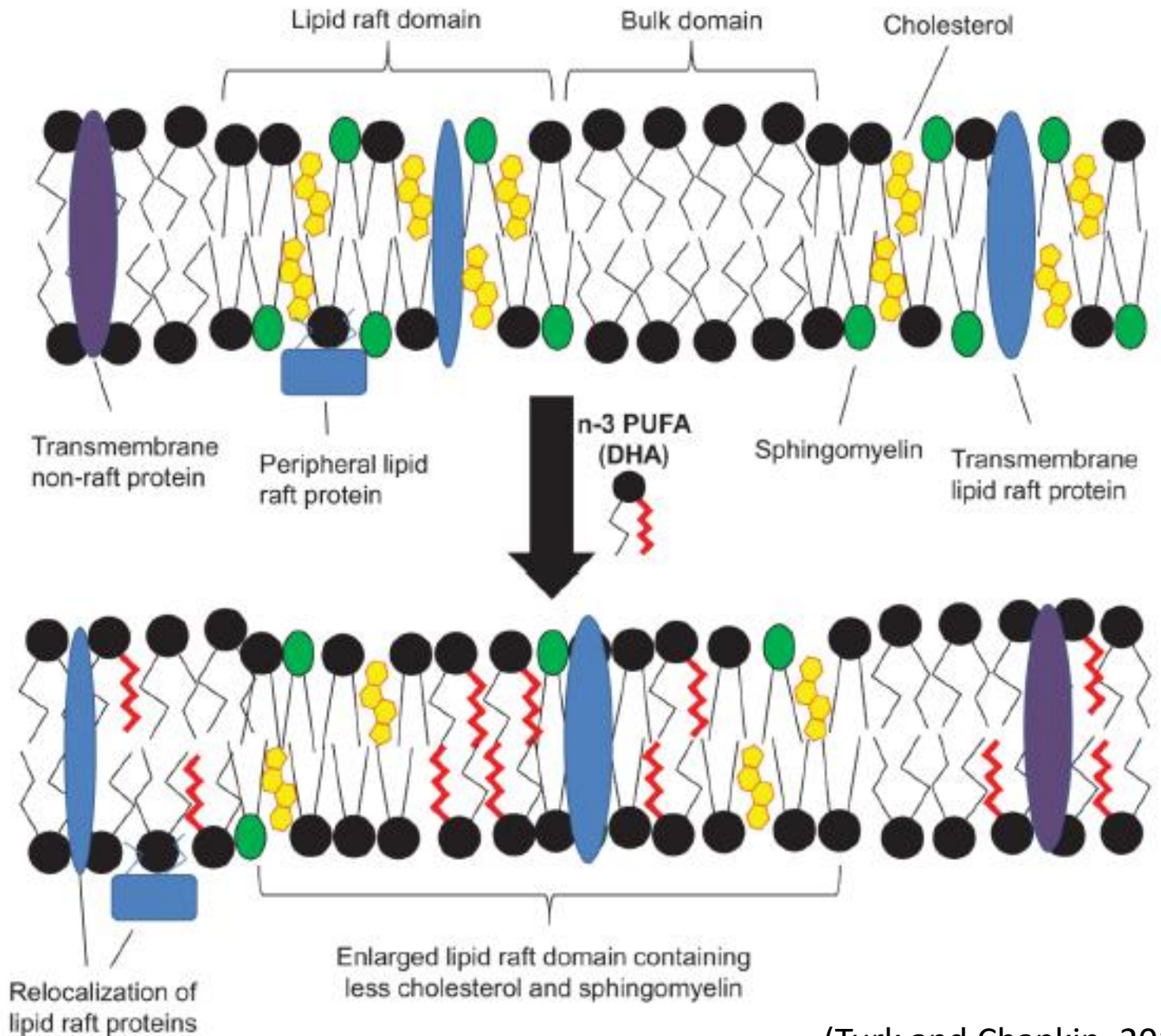
S. J. Singer and Garth L. Nicolson

SCIENCE, VOL. 175



*“The bulk of the phospholipid is organized as a discontinuous, fluid bilayer, although a small fraction of the lipid may interact specifically with the membrane proteins.”*

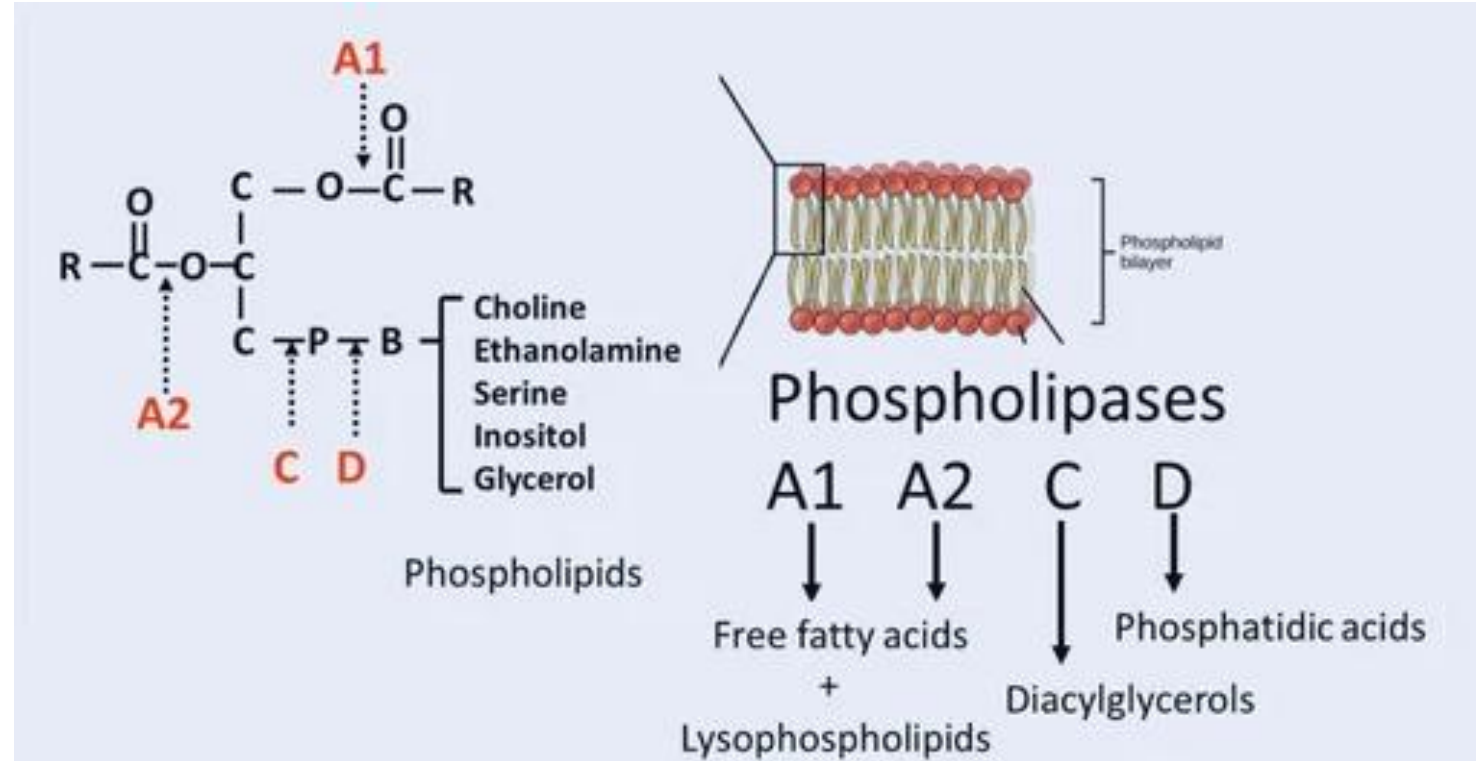
- **Simons and van Meer (1988)** suggested existence of microdomains or “rafts” in plasma membrane
- **Cholesterol-rich microdomains that regulate diverse range of cellular functions**
- **Rich in cholesterol and sphingolipids**
- **Crucial for neural development and function**
- **Many disease such as AD, are related to lipid rafts**

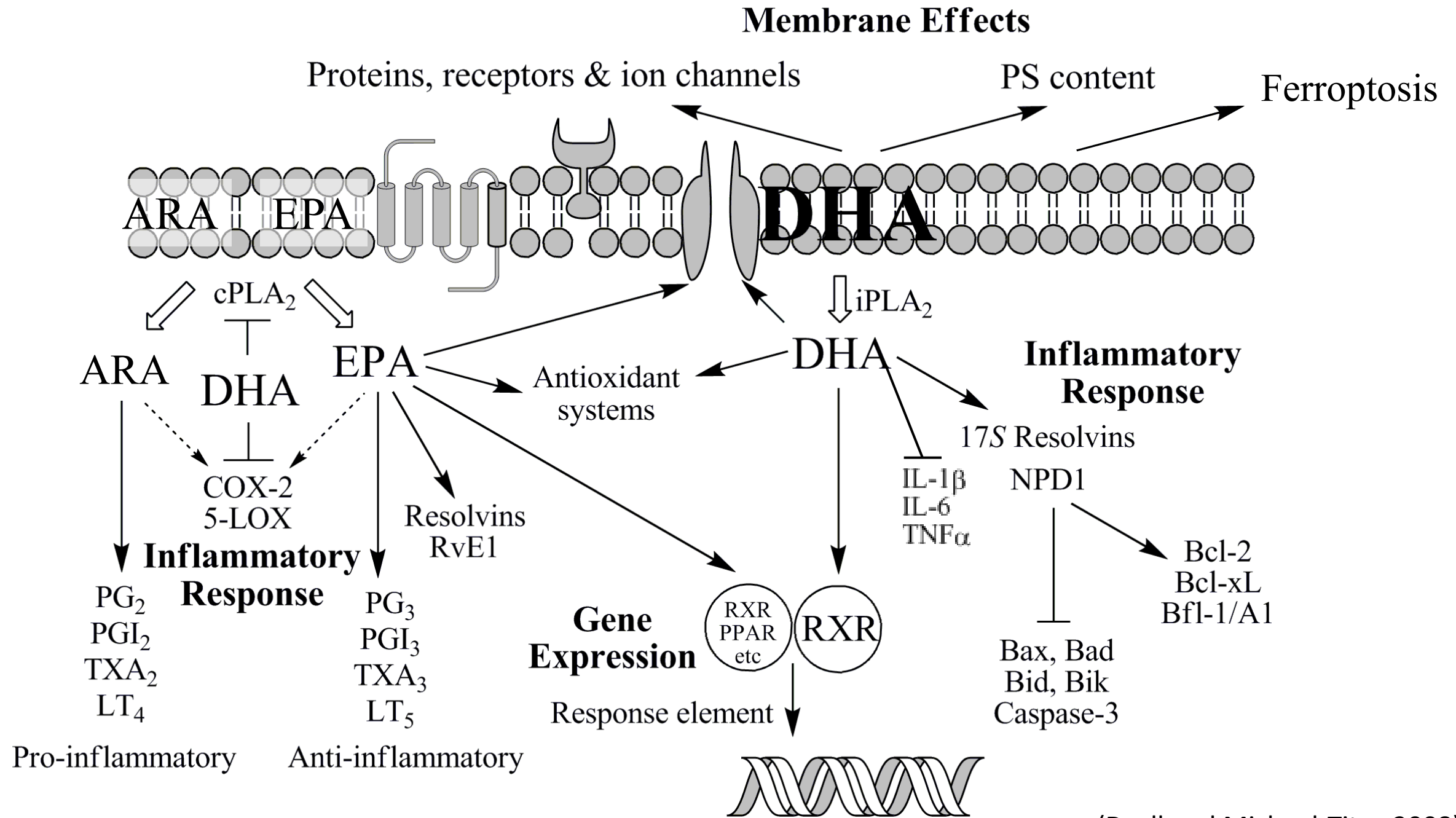


(Turk and Chapkin, 2013)

# Second Messengers

- In response to a variety of hormones or neurotransmitters, PLs break down via action of phospholipases:
  - *Phospholipase A*
  - *Phospholipase C*
  - *Phospholipase D*





# The Brain is Made of Fat

Brain 55% lipid, GM 35-40%, WM 50-66% and myelin 80%

(O'Brien and Sampson 1965)

## 1. Cholesterol

## 2. PLs

- Phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylinositol (PI), and phosphatidylserine (PS)

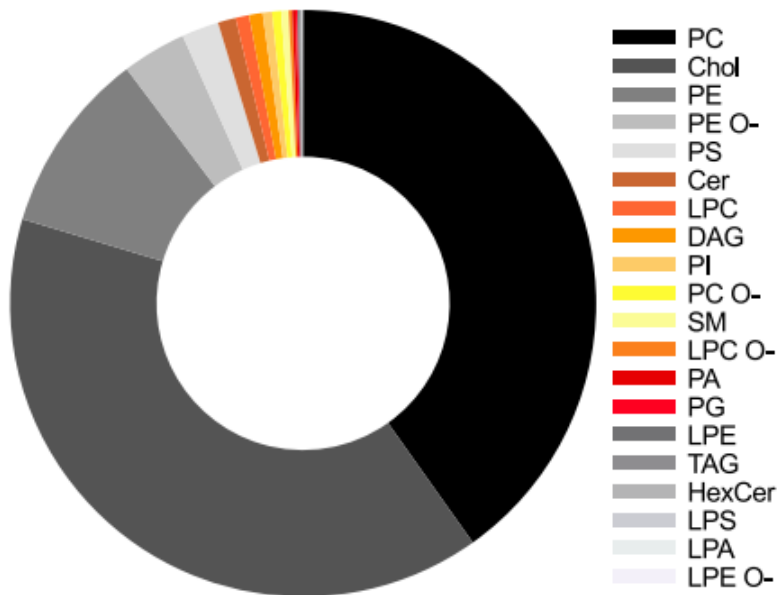
## 3. Sphingolipids

- Sphingomyelin (SM), cerebroside, ceramide (Cer), sulfatide (Sulf), and ganglioside

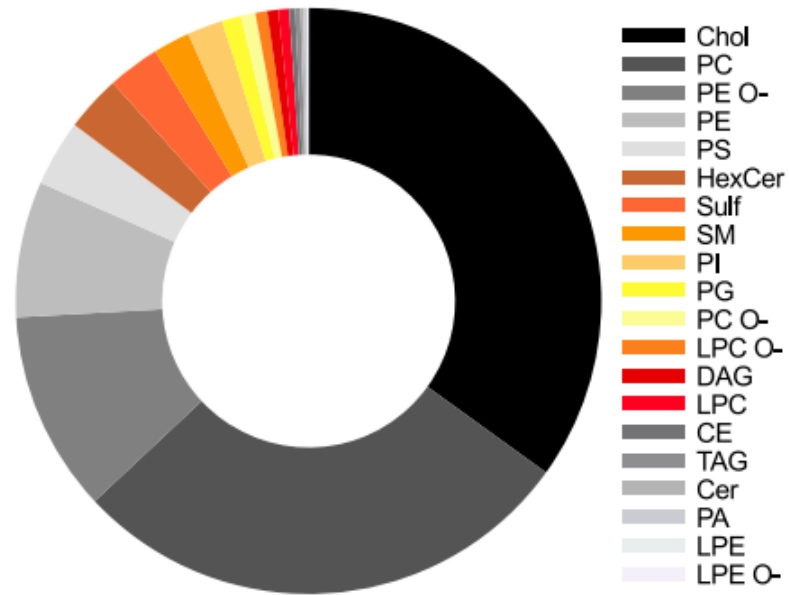


(Jackson *et al.*, 2005)

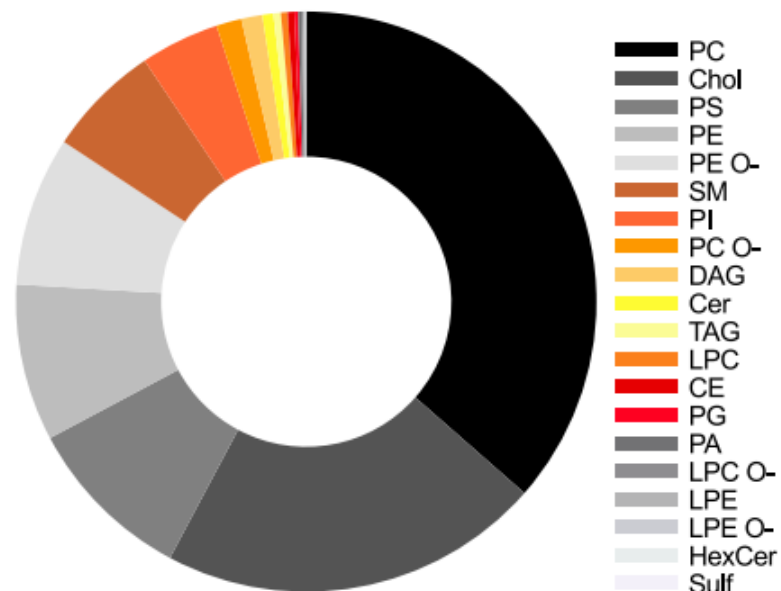
neurons



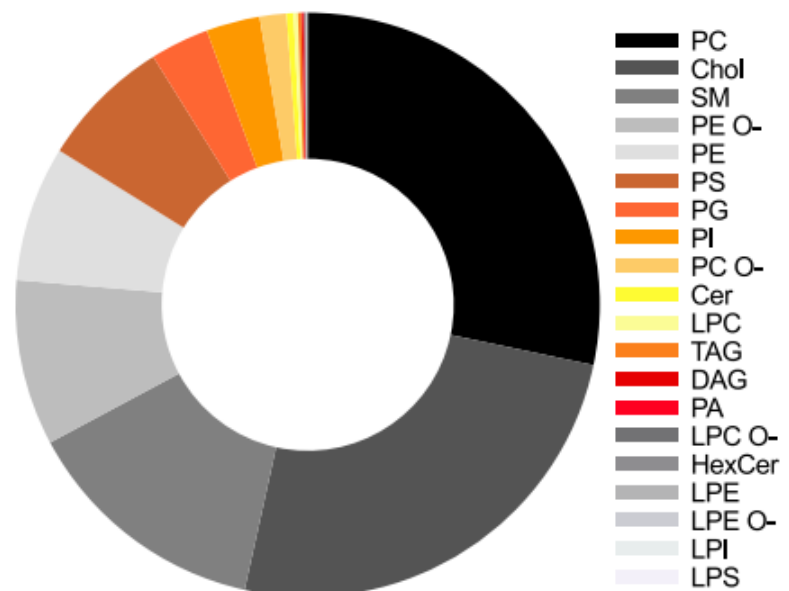
oligodendrocytes



astrocytes



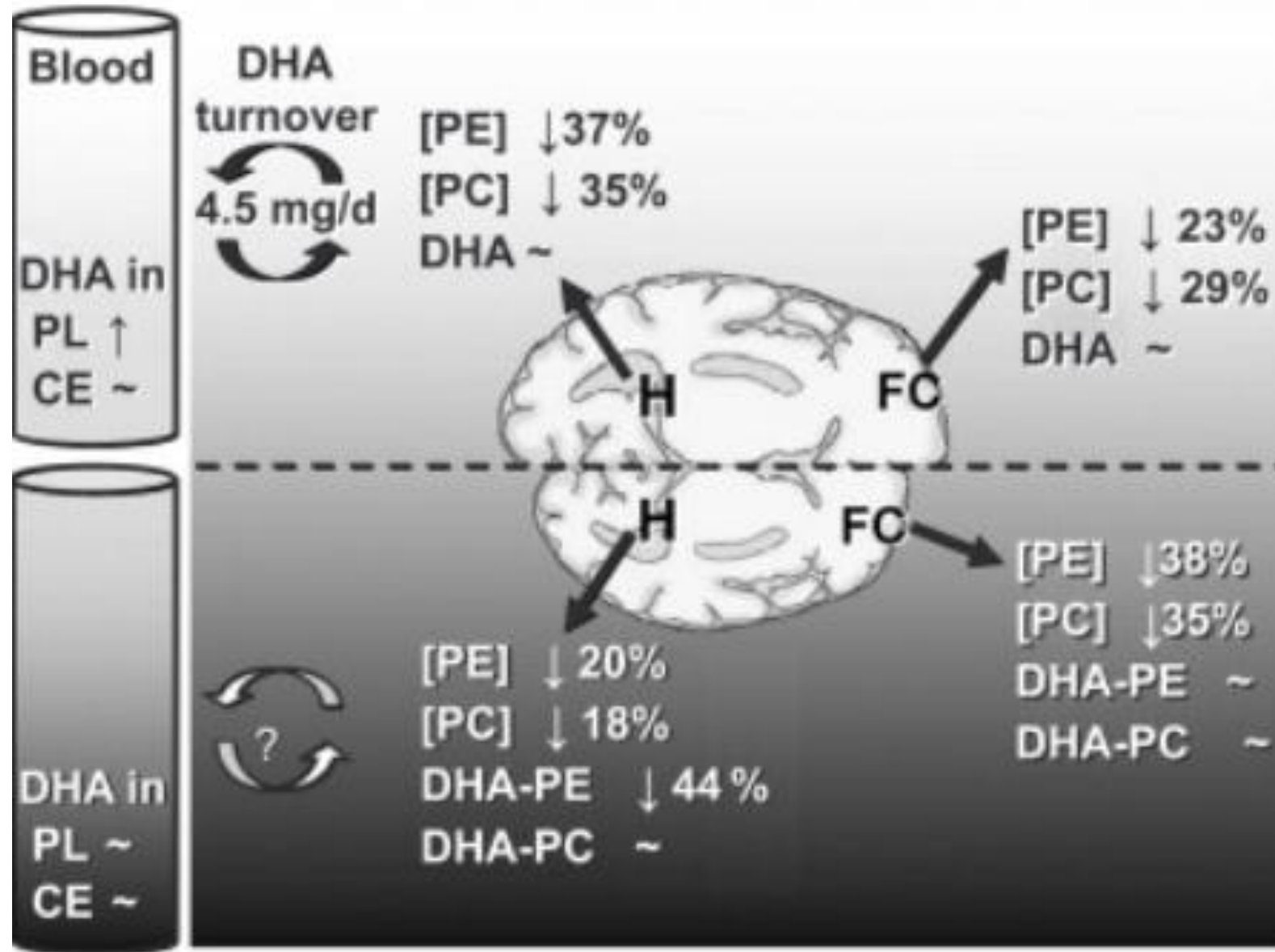
microglia



***3. Do PL levels change?***

Lipid class	Change/Normalization	Sample size/Examined brain regions/Analytical method	Reference
PI	decreased/wet weight	9 AD and 9 controls/HPG, SMTG, IPL and cerebellum/TLC	[14]
PI	decreased/wet weight	17 AD and 18 controls/anterior temporal cortex/TLC	[15]
PI	decreased/relative	45 AD and 11 controls/SMFG, STG, IPL, occipital cortex and cerebellum/ <sup>31</sup> P NMR	[21]
PE	decreased/wet weight	9 AD and 9 controls/HPG, SMTG, IPL and cerebellum/TLC	[14]
PE	decreased/DNA	10 AD and 10 controls/frontal, primary auditory and parietal cortex/photometrical phosphorus determination	[16]
PPE	decreased/relative	9 AD and 9 controls/middle-temporal cortex/HPLC and TLC	[18]
PPE	decreased/phosphate	15 AD and 13 controls/frontal cortex, hippocampus and white matter/HPLC and GC	[19]
PPE	decreased/relative	45 AD and 11 controls/SMFG, STG, IPL, occipital cortex and cerebellum/ <sup>31</sup> P NMR	[21]
PPE	decreased/protein	6 CDR = 0; 6 CDR = 0.5; 6 CDR = 1; 6 CDR = 2; 6 CDR = 5/white and gray matter from SFG, STG, IPL and cerebellum/ESI-MS	[22]
PC	unchanged/wet weight	9 AD and 9 controls/HPG, SMTG, IPL and cerebellum/TLC	[14]
PC	decreased/DNA	10 AD and 10 controls/frontal, primary auditory and parietal cortex/HPLC-fluorimetric detection	[16]
PC	unchanged/wet weight	6 AD and 4 controls/gray matter from frontal cortex, parietal and temporal region/HPLC	[17]
PC	decreased/phosphate	15 AD and 13 controls/frontal cortex, hippocampus and white matter/HPLC and GC	[19]
SM	decreased/protein	9 AD and 6 controls/gray matter from frontotemporal area/enzymatic assay-HPLC	[24]
SM	decreased/relative	7 AD and 7 controls/MFG, SFG and cerebellum/ESI-MS	[25]
SM	increased/relative	30 AD and 26 controls/MFG, MTG and cerebellum/ESI-MS	[26]
SM	increased/relative	45 AD and 11 controls/SMFG, STG, IPL, occipital cortex and cerebellum/ <sup>31</sup> P NMR	[21]

# Healthy Elderly



# Alzheimer's Disease

# Changes with AD

- **↓ PC and PE (PE-plasmalogens)**
  - PCs and PEs show variation in SFA:PUFA and DHA
- **↓ PI**
  - Disruptions in production and signalling pathways
- **Loss of PS asymmetry**
  - ↑ Externalization to outer leaflet under oxidative stress
- ***Evidence that most, if not all, classes of PLs are implicated in the pathology of AD***

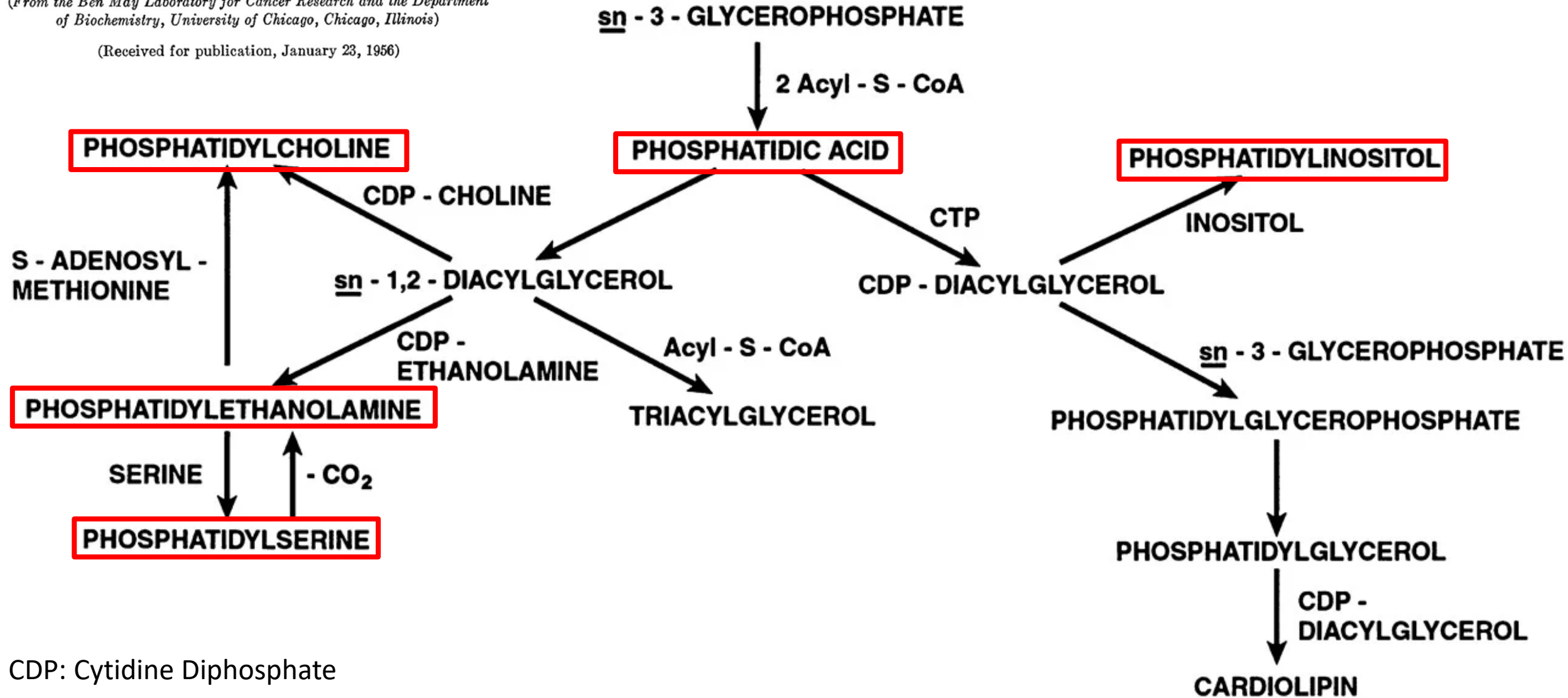
***4. How are PLs made and can they be increased?***

THE FUNCTION OF CYTIDINE COENZYMES IN THE BIOSYNTHESIS OF PHOSPHOLIPIDES\*

BY EUGENE P. KENNEDY AND SAMUEL B. WEISS†

(From the Ben May Laboratory for Cancer Research and the Department of Biochemistry, University of Chicago, Chicago, Illinois)

(Received for publication, January 23, 1956)



CDP: Cytidine Diphosphate

CTP: Cytidine Triphosphate

# Can PL formation be increased?

World Rev Nutr Diet. Basel, Karger, 2009, vol 99, pp 71–96

## Administration of Docosahexaenoic Acid, Uridine and Choline Increases Levels of Synaptic Membranes and Dendritic Spines in Rodent Brain

Richard J. Wurtman<sup>a</sup> · Mehmet Cansev<sup>a,b</sup> · Toshimasa Sakamoto<sup>a</sup> · Ismail H. Ulus<sup>a,b</sup>

**Table 3.** Effects of giving UMP-supplemented diet (0.5%) and DHA (300 mg/kg) on phosphatide levels in different gerbil brain regions [data from 14]

	Cortex	Striatum	Hippocampus	Brain Stem	Cerebellum
<b>Total PL</b>					
Control diet + Vehicle	267	265	264	450	270
UMP diet + DHA	316**	339***	314**	521**	317**
<b>PC</b>					
Control diet + Vehicle	94	100	102	114	98
UMP diet + DHA	122***	126*	117***	139***	111***
<b>PE</b>					
Control diet + Vehicle	58	60	61	117	64
UMP diet + DHA	80**	85***	81***	156***	85***
<b>PS</b>					
Control diet + Vehicle	24	24	24	30	24
UMP diet + DHA	30***	29*	28***	35***	29**
<b>PI</b>					
Control diet + Vehicle	10.6	7.6	8.8	9.3	10.4
UMP diet + DHA	13.2**	11.9***	11***	11.8*	11.5*

Component	Amount per daily dose*
EPA	300 mg
DHA	1200 mg
Phospholipids	106 mg
Choline	400 mg
UMP (uridine monophosphate)	625 mg
Vitamin E (alpha-TE)	40 mg
Vitamin C	80 mg
Selenium	60 µg
Vitamin B12	3 µg
Vitamin B6	1 mg
Folic acid	400 µg

Abbreviations: EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; TE, tocopherol equivalents.

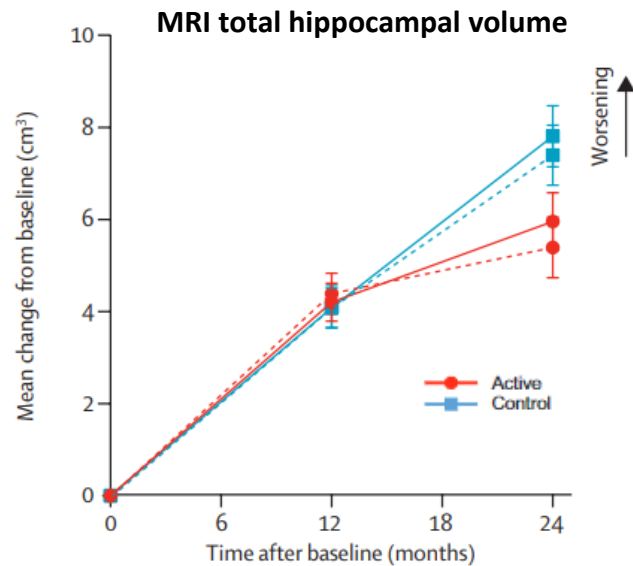
\*Souvenaid (125 mL daily dose) contains Fortasyn Connect.

# LipiDiet Clinical Trial

## 24-month intervention with a specific multinutrient in people with prodromal Alzheimer's disease (LipiDiDiet): a randomised, double-blind, controlled trial

*Lancet Neurol* 2017; 16: 965-75

Hilkka Soininen, Alina Solomon, Pieter Jelle Visser, Suzanne B Hendrix, Kaj Blennow, Mii Kivipelto, Tobias Hartmann, on behalf of the LipiDiDiet clinical study group\*



Received: 9 January 2020 | Revised: 10 July 2020 | Accepted: 14 July 2020

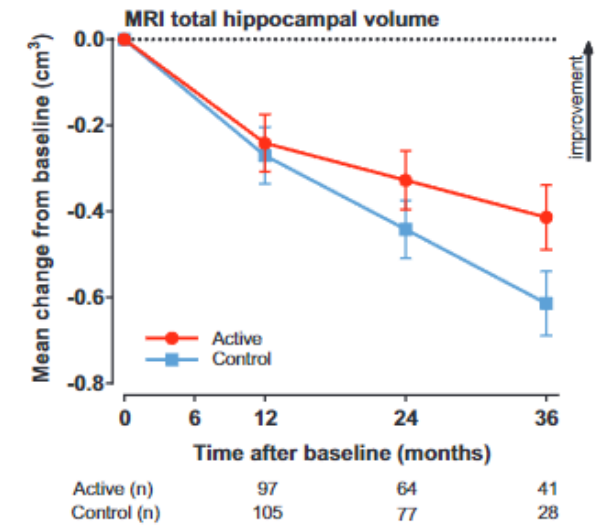
DOI: 10.1002/alz.12172

Alzheimer's & Dementia®  
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

### RESEARCH ARTICLE

## 36-month LipiDiDiet multinutrient clinical trial in prodromal Alzheimer's disease

Hilkka Soininen<sup>1,2</sup> | Alina Solomon<sup>1,3,4</sup> | Pieter Jelle Visser<sup>5,6</sup> | Suzanne B Hendrix<sup>7</sup> | Kaj Blennow<sup>8,9</sup> | Mii Kivipelto<sup>1,3,4,10,11</sup> | Tobias Hartmann<sup>12,13</sup> | on behalf of the LipiDiDiet clinical study group



# Summary and Conclusions

- **PLs have essential cellular structural and functional roles, and are a reservoir of omega-3 and omega-6 PUFAs**
- **Ageing induces complex changes in lipid (PL) profiles across different brain regions**
  - Can affect brain function and contribute to neurodegenerative diseases, such as AD
  - ↓ PC and PE (PPE), and changes in fatty acid composition
  - *Dietary supplementation may lead to increased PL levels*