NEWSLETTER

PHOSPHATIDYL SERINE

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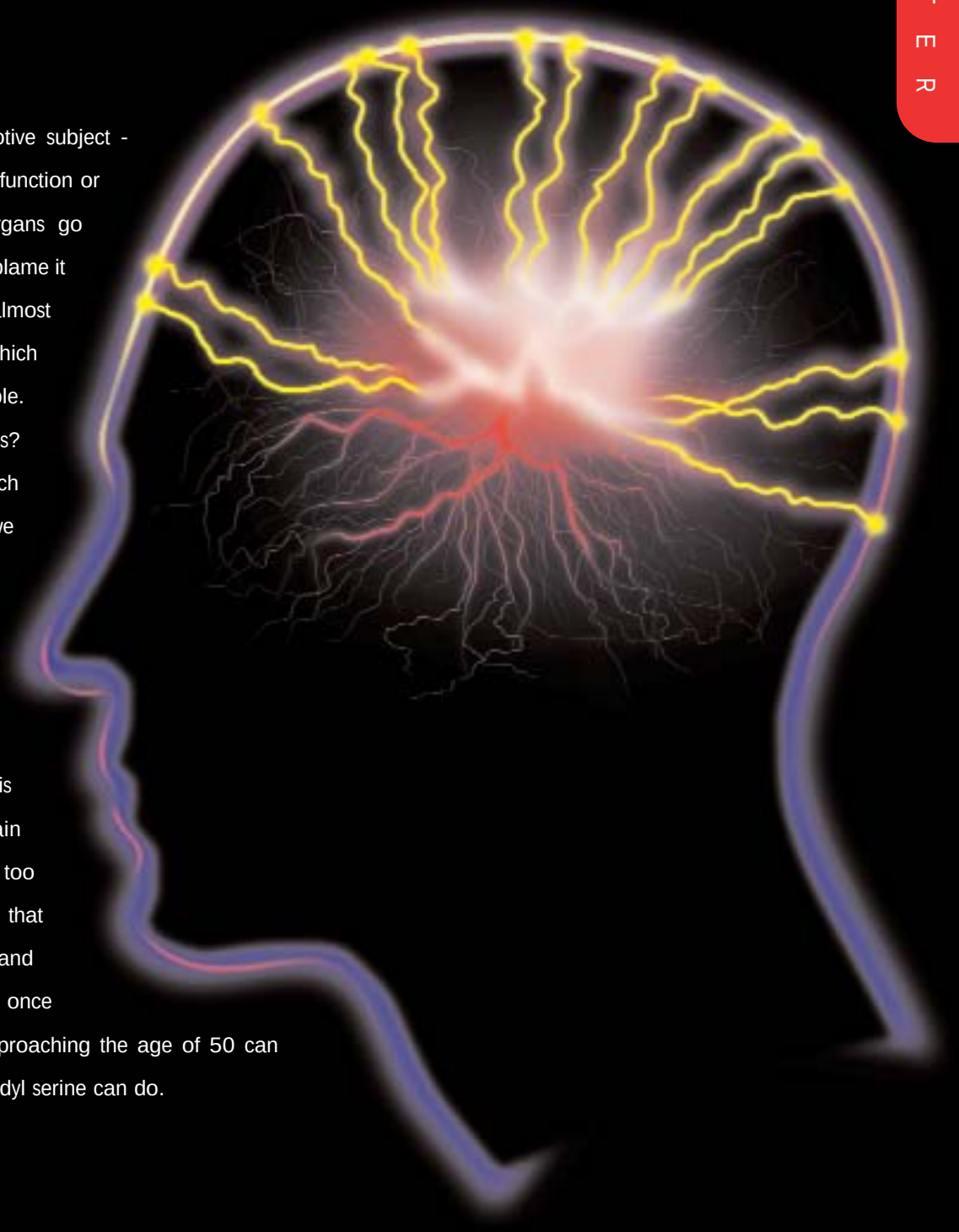

Brain function is rather an emotive subject - much more so than, say kidney function or liver function. If the latter organs go wrong we are quite likely to just blame it onto "my kidneys" or "my liver", almost as if these were spare parts for which we do not feel wholly responsible. Can we do that with our brains? Well, not really, they are too much part of our inner being. Unless we want to verge onto the religious and speak of the "spirit" then, in a worldly sense, our brain is us and we cannot separate ourselves from it. We hate to admit there is anything wrong with our brain function because that is far too personal! Yet many of us know that memory, learning, cognition and recall are no longer all that they once were. No-one who is even approaching the age of 50 can afford to neglect what phosphatidyl serine can do.

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Years ago, a friend of the author, who is an obsessional intellectual, declared that if the technology could be developed to do it, he would quite like to live out his life just as a brain - surviving upon nutrients in a pot - being fed information and images which he could in some way process and then output back to the world. He, without a doubt, was an unusual case - a scientist, philosopher, and lawyer-cum-politician all rolled into one. Clearly, he regarded his brain as his only useful organ and his body as an encumbrance. I think he quite neglected the fact that he would have to depend upon people with bodies to service his brain's nutritional requirements and to maintain the correct ambient conditions. Most of us would not go that far, but few of us would deny that the efficient function of our brain is basic to our enjoyment of and fulfilment in life. How many of us could really say that we always find our brain function optimal?

The realisation that the well-being of the brain is just as dependent - or more so - upon good nutrition as the rest of the body is fairly recent. Ever since the discovery of vitamins, such as vitamins A and C, and the awareness that the oxygen-carrying capacity of the blood depends upon iron, it has been obvious that the functions of other organs and tissues were directly dependent upon nutrients, but somehow the brain was left out of the picture for many years, as if its function was independent of everything. Now we know that is far from the truth because the brain cells have a very great degree of sensitivity to their pattern of nutrient supply. We also know that they stand in critical need of certain specific nutrients which are often less critical for other tissues. Amongst these, the nutrients that are required to maintain the special properties of the membranes of the nerve cells, are of unique importance. These tend to be substances of a fatty nature - but not just ordinary fats. By 1990 it was clear that laboratory rats that were normally bright mentally when it came to running mazes and other rat brain-teasers, became really dull and stupid when deprived of the correct balance of dietary fatty acids. This was perhaps a clear indicator that the make-up and properties of the nerve cell membrane was really vital to function

WHAT IS PHOSPHATIDYL SERINE?

Phosphatidyl serine is one of a group of substances known as "Phospholipids". Other well known examples are Phosphatidyl Choline and Phosphatidyl Inositides. These latter two have important functions throughout the body, whereas the role of Phosphatidyl Serine is concentrated upon the brain. It is now apparent that Phosphatidyl Serine is so very important to the structure and function of the brain cell membrane that the whole functioning of the brain cells is adversely affected when they lack the proper amounts of it.

WHAT IS ITS NATURE AND COMPOSITION?

The "Phosphatidyl" part contains a structure quite like a fat, but with phosphoric acid attached to it. The "Serine" part comprises an amino acid, and quite a common one at that. Indeed, both these parts can usually be made readily enough in the body. Neither of them are "essential" nutrients in the sense of having to take them in ready-made in the diet. When our bodies are young enough and sufficiently non-toxic, they can make quite enough phosphatidyl serine. *What we have to appreciate is that the biochemical processes which form phosphatidyl serine in the body from its component parts are energy-demanding processes*. They are all right so long as our cells go on making enough cell energy to fuel this process adequately. As soon as the energy-generation inside the body cells is slowed down or compromised by ageing - or by the presence of toxins and toxic damage - which are much the same thing - then creating new supplies of phosphatidyl serine becomes difficult. This event is associated with the age of the person. That is no surprise because as we get older, we are accumulating more toxins and toxic damage. However, it is not solely related to age. Undue toxic exposure at an earlier age can sometimes produce a similar result.

WHAT WILL PHOSPHATIDYL SERINE DO?

What phosphatidyl serine has been found to do can be described as "improving cognition". A dictionary definition of "cognition" is "knowledge, apprehension, knowing, in the widest sense, including sensation, perception etc.". One might well, therefore, sum it up as "mental grasp": some would say "being on the ball". However, important parts of "cognition" not covered by the dictionary definition have to do with memory and memory recall. It is all very well being able to perceive and grasp information when you first see it, but what about recalling it afterwards? The concept of mental grasp is actually very broad. One would certainly expect it to translate readily enough into the ability to do mental arithmetic, write difficult letters, do accounts, recite evidence in a court of Law. However, the things which have actually been measured do reflect several of its many aspects, including, perception, memory of what was perceived, and recall, including the ability to match what is seen now with what was seen some time ago.

The mental functions which have been studied and documented in trials include learning names and faces, recalling names and faces and matching recalled faces to recalled names. To that can be added, the recalling of telephone

numbers, recalling the position of misplaced objects (how many of us have difficulty with that?), recalling paragraphs read, ability to concentrate upon reading and performing tasks. The list continues with recalling events of the previous day or of the past week.

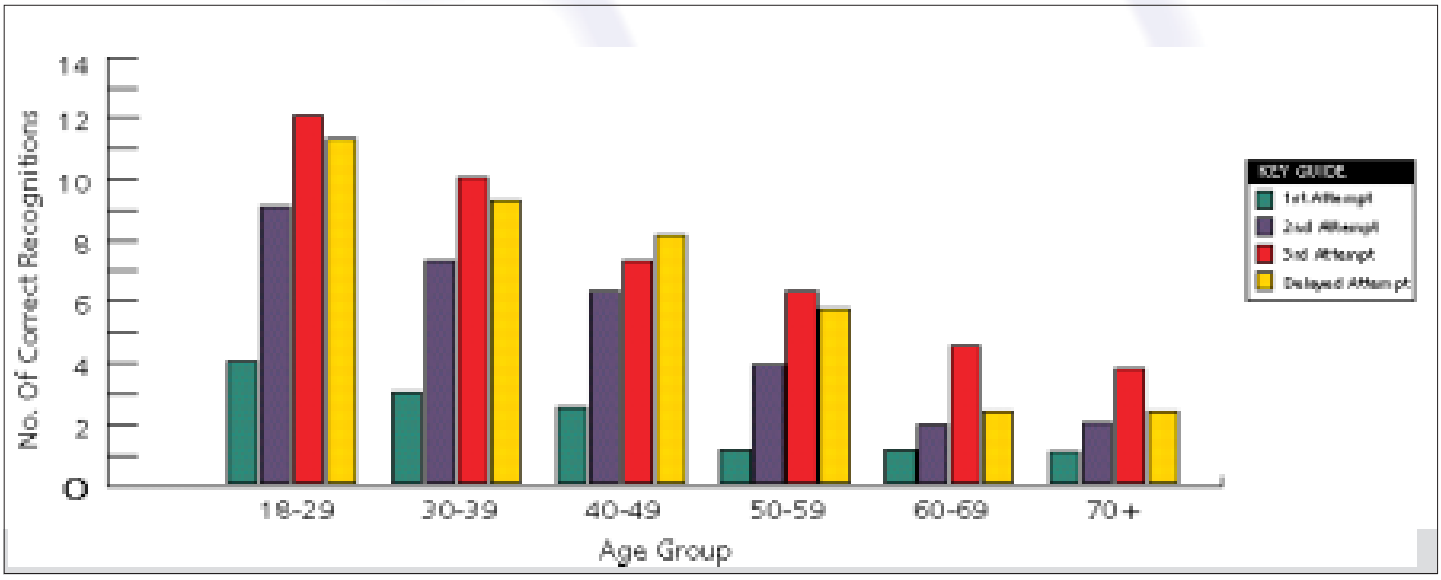
More general functions reported as being improved by phosphatidyl serine include mood and attentive function, behaviour and social interest and participation, avoidance of apathy and withdrawal, improvement of sleep patterns, better vigilance, better motor reaction (an example of this would be putting on the car brakes in an emergency or catching a ball) and, in the elderly, increased self-sufficiency in daily living.

WHAT IS THE EVIDENCE THAT PHOSPHATIDYL SERINE WILL DO ALL THIS?

The evidence has been amassed principally during the years 1986-1993 through conducting controlled clinical trials both in Europe and the United States. In Europe they have included work done at the University of Liege in Belgium and at least five trials in Italy, one of which involved three clinics working in collaboration. One of the Italian trials was both large and long, involving 425 subjects ages 65-93 recruited at 23 institutions throughout northern Italy, and it was maintained for 6 months. The two US trials both involved Dr T.H. Crook of the Memory Assessment Clinics (MAC) of Bethesda, Maryland. In one they worked with the University School of Medicine at Nashville, Tennessee and the University School of Medicine in Palo Alto, California and Fidia Pharmaceutical in Italy. The second involved MAC in conjunction with the Nashville School and ExPharma of Italy. Between them these eight studies established all the findings listed in the last paragraph. They did so in most cases with a high level of statistical assurance that the conclusions were reliable. These are not the only trials that have been run by any means, though they are probably the most significant. In all some 42 scientific studies have been reported upon the use of phosphatidyl serine in relation to cognitive brain functions, of which 17 were double-blind trials. The use of the double-blind method, in which neither the subject nor the doctor knows whether the particular subject is getting the trial compound or a placebo until after the results have been noted, is considered to greatly increase the value of information gained from the trial.

HOW BIG ARE THE EFFECTS?

All the indications are that the effects of taking phosphatidyl serine regularly are considerable and impressive, certainly enough to make a real difference to a person's performance of tasks or to their enjoyment and fulfilment in life. For example, in the first of the American trials, mental function, as measured by the one simple test of learning names and faces, the performance of the tested group of individuals improved so much that a person of age 64 performed at the level normally associated with someone of 52. In other words, in terms of cognition and learning, the clock had been rolled back some 12 years. In the American studies improvement in mental ability were noted within as little as three weeks from starting to take phosphatidyl serine. Both American studies confirmed that phosphatidyl serine can benefit particular aspects of cognitive functioning in mildly impaired individuals. In four different tests of the ability to store and recall information, especially long-term storage and recall, used in one of the Italian trials, there was a 10-30% improvement in performance after six months use of phosphatidyl serine. There is every reason to think that with longer term use and, especially with people who begin the use of phosphatidyl serine at a younger age, considerably bigger effects than this can be expected.



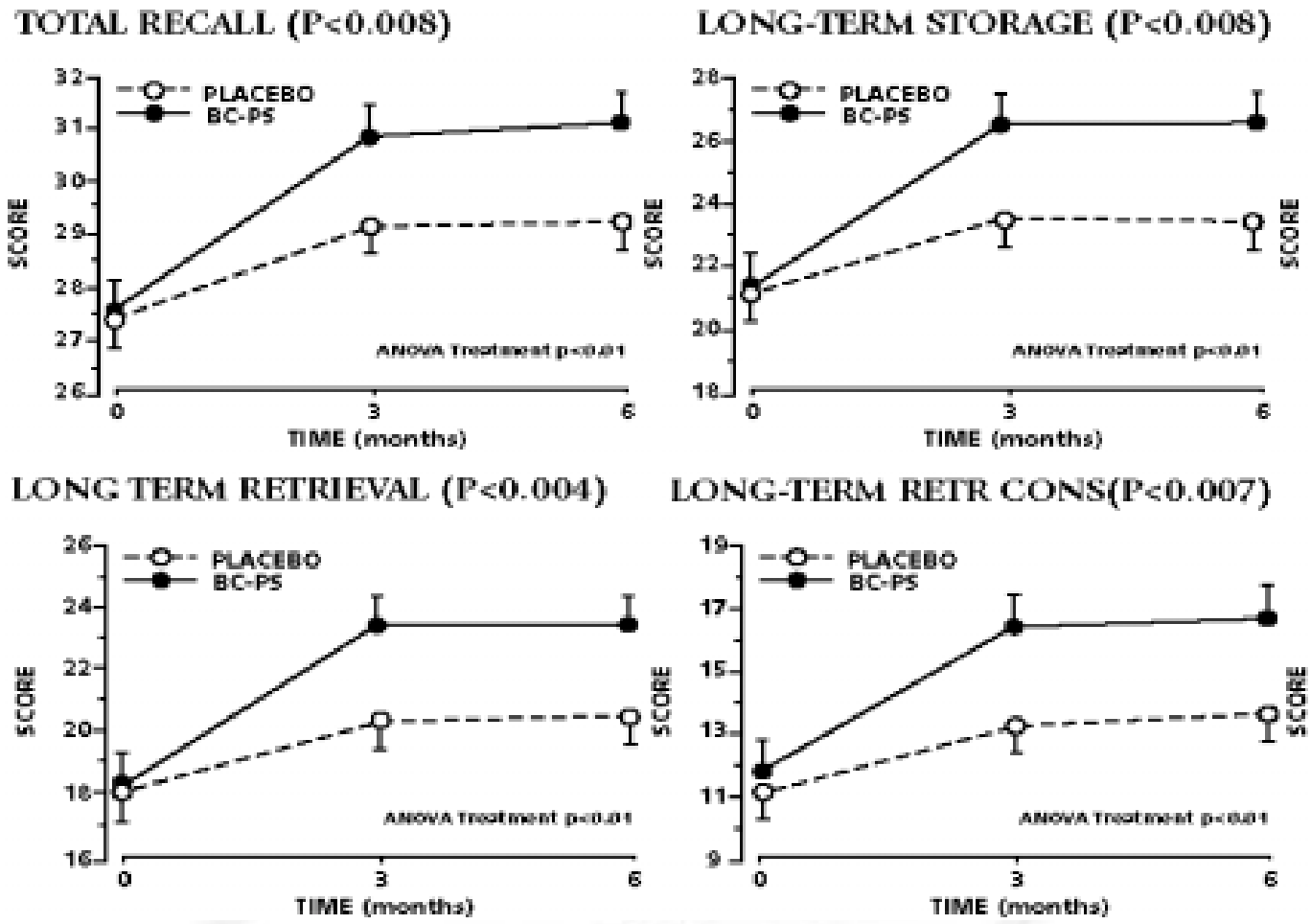


Figure 1 graphs these improvements from the trials. Benefits of PS on measures of ***Total Recall****,* ***Long-Term Storage****,* ***Long-Term Retrieval****, and* ***Long-Term Retrieval Consistent****. From Cenacchi et al. (1993)*

It has not been practical to run the human trials for more than six months, but the work done with animals, such as rats, with a much shorter life span, gives an indication that long term intake will produce far bigger effects. The ageing rat becomes mentally senile, just as humans do, losing its "sharpness" in maze-running, etc. It also shows very marked death of brain cells as the rat ages, just as in humans. Yet the brain function of the aged rat is very largely renewed and restored by giving enough phosphatidyl serine for long enough. At the same time, by examining the rat's brain tissue in the laboratory, you can see that the brain cells are being spared. In fact, the reports say that there is almost 100% brain cell conservation in the rat when it is given phosphatidyl serine from a sufficiently early age.

HOW DOES IT WORK IN THE BODY?

Laboratory studies have shown that phosphatidyl serine supports the brain cells in a number of different ways. Because phosphatidyl serine is active at the cell membrane and at various structural membranes inside the cell, it is presumed that a good many of its functions are the result of supporting membrane function. It is clear that phosphatidyl serine promotes efficient transmission of messages across the junctions between one nerve cell and another. It also promotes the production of a nerve cell growth factor, which is a chemical messenger promoting the health, well-being and active life of brain cells. The outcome is that the metabolic rate of the brain cells is stimulated, and hence they use more oxygen. As a result, the blood supply to the brain is increased, in response to increased demand from the activated brain cells. This effect can be demonstrated using a special colour-imaging technique called P.E.T. This shows up in brilliant colour the areas of the brain which exhibit good levels of activity at the time of the scan. Using this tool, the results of taking phosphatidyl serine are quite dramatically visualized.

CAN WE GET IT FROM FOODS?

There are only very low levels in food, even in soya, which is such a good source of other phospholipids. This means that human requirements are normally met by new synthesis of phosphatidyl serine in our own bodies. Yet this fact leaves us exposed when our ability to make phosphatidyl serine deteriorates.

WHAT DAILY INTAKES ARE NEEDED?

Most of the trial work was done with a daily intake of 300mg, which was often given in the form of a 100mg capsule or tablet three times daily. This would be an ideal dose to obtain fully the benefits reported in the various trials. In one trial 500mg per day was used. However, users may wish to try doses from 100mg / day upwards, regarding 400mg as a maximum. This may suit particularly those with only minor problems, or applying it only for preventative use.

WHAT ARE PHOSPHATIDYL SERINE'S OTHER EFFECTS?

In addition to the applications already discussed, phosphatidyl serine has also been reported to reduce stress hormone production during very heavy exercise or athletic performance, to increase a person's ability to withstand stress, and to reduce clinical depression. It is also reported to improve childhood hyperactivity (attention deficit hyperactivity disorder).

FROM WHERE ARE PHOSPHATIDYL SERINE SUPPLEMENTS OBTAINED?

Their origin is generally from the soya bean. This is so, notwithstanding the low content of phosphatidyl serine normally in soya beans, because, in the manufacture, the soya bean material is put through a special enrichment process. This means that the phosphatidyl serine itself is likely to be entirely acceptable to vegetarians, though whether that is also true of tablets or capsules which contain it, depends upon whether or not any gelatine or non-vegetarian excipients have been used. It is possible to check with the manufacturer whether or not genetically modified soya bean has been excluded.

SAFETY AND ABSORPTION

The experience of the large number of trials that have been conducted with phosphatidyl serine and the large numbers of subjects involved in those trials, represents a very real safeguard against side effects. No such effects of any significance were noted during those trials. Phosphatidyl serine is also very available in the human when taken by mouth, as its absorption and utilization are good.

SUPPLEMENTARY NUTRIENTS TO USE WITH PHOSPHATIDYL SERINE

All the available evidence shows that phosphatidyl serine is entirely capable of producing the reported benefits without having to be accompanied by anything else. The published trials have in general been kept simple and the use of multiple supplements has been avoided. However, when it comes to producing the highest benefits we possibly can to the brain function of a particular individual, it makes every sense to pull together all the different factors that will contribute. Here one does well to view the brain cell as being an entire nutritional entity. Phosphatidyl serine is obviously uniquely crucial, as all the foregoing information shows. However, it needs, in addition, all the general nutrients that are required by other cells. Its well-being depends upon those too. In an excellent book by Jean-Marie Bourre, "Brainfood", published in 1990 (1993 - English translation) the various common nutrients are reviewed for their positive actions upon brain function. In this context, we can regard them as being nutritional adjuncts to the crucial and central actions of phosphatidyl serine. They work by under-pinning the general health of the brain cell. None of them is remotely capable of replacing phosphatidyl serine, but they are all capable of supporting their actions. On the basis of this one can recommend the following as supportive adjuncts, for those cases that really need them.

1) A good quality multimineral. At best it should be able to deliver the recognised "Reference Nutrient Intake" of each of the trace minerals, zinc, copper, manganese, selenium, chromium, molybdenum, with iron being necessary or not, depending upon whether the patient has a recognisable deficiency.
2) An organic source of magnesium, delivering not less than 300mg per day.
3) A complex of B Vitamins
4) An anti-oxidant formula, or single supplements, comprising at least Vitamin C (500mg / day), Carotene (15mg / day) and Vitamin E (200i.u. / day). The effect of these may be even better if further anti-oxidants are added, such as Co-Enzyme Q10.
5) High quality Linseed Oil or Fish Oil, to give 2g of α Linolenic acid or EPA per day.

Not everyone will absolutely need all these extra nutrients. Also, we do not have definite proof of the specific extra benefits from adding these nutrients over and above phosphatidyl serine, but we do have clear proof that they are, indeed, brain nutrients in their own right, and can influence performance.

CONCLUSION

The results from the numerous trials on phosphatidyl serine overwhelmingly indicate that it is a promising and thoroughly safe dietary supplement, efficacious in producing the various benefits that have been described. Finally, although the body, in health, can manufacture it, the energy cost of doing so is high and the compromised or energy-deficient system is unable to produce it in sufficient amounts to maintain the brain cells and other nervous system cells in good condition.

FOOT NOTE ABOUT WORKING WITH ANIMALS

This author stresses that neither he nor Biomedical Information Services are involved in animal studies of any kind. The references we make to any such work are provided for information only and we in no way condone such experiments.

APPENDIX 1

NOTES UPON P.E.T. IMAGING

PET is a special technique called Positron Emission Tomography and it is capable of showing up the energy states of the various different parts of the brain. The chart it produces is a colour-coded "map" of the brain. Some of the colours (the lighter, brighter colours) represent higher energy states, while the duller, darker ones represent lower energy conditions. What do we mean by "energy states"? Well, what the PET technique really reveals is the rate of glucose metabolism, oxygen consumption, or other indexes of the rate at which cellular energy is being generated. Experience tells us that the energetically sluggish brain has sluggish inefficient functions and that faster metabolism goes with smarter brain function. The technique has been developed and improved to the point where the contrasts shown up by these "maps" can be dramatic, cover the whole of the brain and provide semi-quantitative colour gradations capable of reflecting quite truthfully various intermediate states of brain activity, not just the extremes. In this way PET and other state-of-the-art imaging methods can help detect and "track" cognitive decline without invading or toxifying the body or seriously inconveniencing the subject under study. This is an exciting development.

Recently it has been demonstrated that cognitive impairment, as seen by poor performance of tasks, goes hand in hand with impaired brain metabolism as revealed by PET. This applied even at the "resting" level, which is the activity level that occurs when no mental test or task is being done. The use of 400mg / day of phosphatidyl serine prevented any further loss in the activity levels of the resting brain. However, interestingly and dramatically, when PET is used to measure brain activity during the actual performance of mental tasks, much greater contrasts are seen between the subject before and after the use of phosphatidyl serine. In other words, the brains of people who had been "primed" with phosphatidyl serine before doing tasks activated and, in terms of PET, "lighted up" far more dramatically than those of unprimed, untreated people.

The colour illustration demonstrates (Figure 3) the changes, via the PET technique, as just described. Note that the colour code bar on the right offers a fairly discriminating visualisation of brain activity. Red represents the highest brain cell activity, the yellow-green colour moderate-to-good brain activity, while the green-blue, through to blue and purple, represent progressive low grade energy states which correlate with poor brain performance.

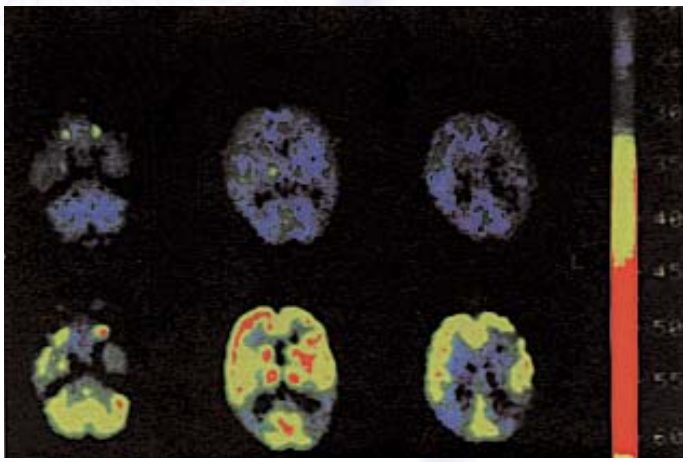


Figure 3

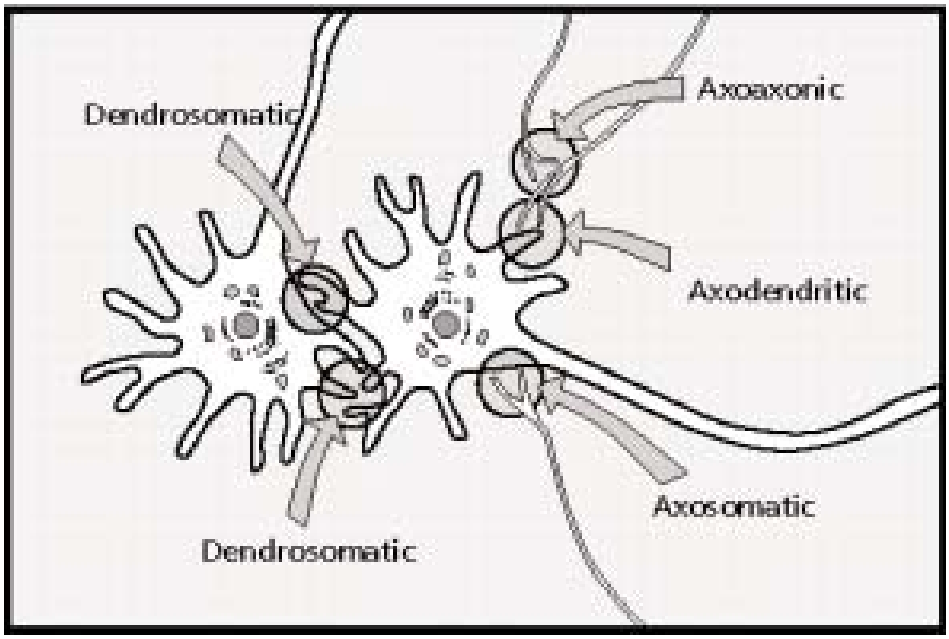
"PET imaging of the brain of a 59-year old woman. The colour scale indicates levels of glucose metabolism / energy production in different brain areas. Upper pictures - before PS: lower pictures - after 500mg PS daily for three weeks. Metabolism is increased in almost all brain regions. See text for colour scale interpretation (After Klinkhammer 1990).

APPENDIX 2

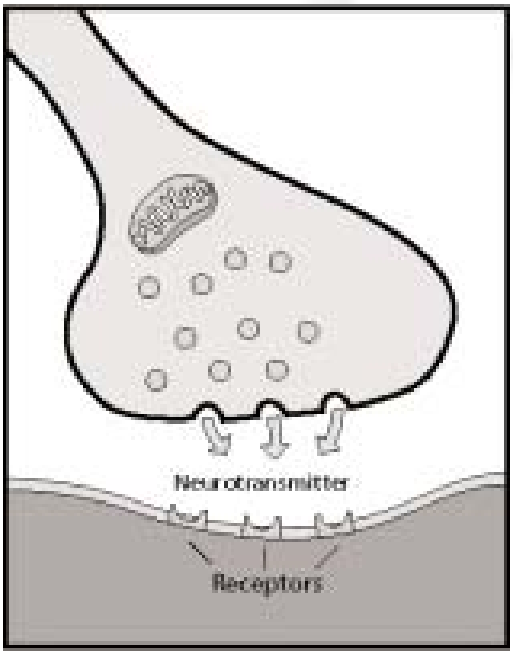
THE PROCESS OF NERVE IMPULSE TRANSMISSION ACROSS THE SYNAPSE

It has been said already that phosphatidyl serine promotes efficient transmission of messages across the junctions between one nerve cell and another. Such junctions are caller "synapses". The brain is most extraordinarily complex mainly because it has so many of these junctions. There are about as many brain cells in the brain as there are stars in our galaxy. Each one may have tens of thousands of cell-to-cell junctions - just as though it were the most complex telephone exchange that ever existed. Hence, brain function is the efficient working of countless billions of these junctions or synapses.

The nerve impulse is conveyed down the length of a nerve fibre electrically. When it comes to the end of the fibre (i.e. end of the cell), it must "jump" a gap - rather like an electric current sparking across a gap. But it does not do this electrically but rather, chemically. A special substance, called a "neurotransmitter" is secreted at the end of one nerve fibre and diffuses quickly across the very small gap to reach and "spark off" the next nerve fibre. In that way the communication is kept going. Phosphatidyl serine, as has been said, facilitates this synaptic transmission. The illustration, Figure 4, shows the structure of synapses between nerve cells in the brain. By reference to Figure, 5, one can see the nature of the process of neurotransmitter release. The end of the nerve fibre which brings the message can be seen in the top half of the picture. It shows small vesicles which act as stores of the neurotransmitter solution. These are membrane-lined spaces containing the solution. The key substances are manufactured in the cell and stored in these vesicles until needed. In order to release the neurotransmitter the vesicle has to migrate to the outer membrane of the cell, fuse with the outer cell membrane, and then open up, releasing the chemical into the narrow space of the synapse.



Types of synaptic connections in the CNS Figure 4



Chemical synapse Figure 5

The reason why phosphatidyl serine has such a major effect upon this process is that it is membrane-active. It positively affects the properties of membranes and the ways in which they work. It does so by favourably influencing the membrane's make-up and character. It therefore can be presumed to influence the nature and behaviour of the vesicle membrane as well as the outer cell membrane. Even the physical properties of the membranes are affected. These membranes - when they work correctly, allow some key substances to pass through whilst others are barred. The membranes also bear some key molecules, called enzymes and "receptors" with very sensitive biological functions. All these factors must be correctly maintained if the process of neurotransmitter storage and release are to function correctly Hence, phosphatidyl serine becomes a guardian of these processes.

APPENDIX 3

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