Overview of the Potential Effect of B Vitamins on Cognitive Health

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Abstract:
B vitamins has a biological role to promote health and cognitive function. There were some studies demonstrated the potential effect of B vitamins in such brain domains e.g. memory and nonverbal thinking. Therefore, the role of B vitamins on the brain is still great potential for further research. However, many studies confirmed the relationship or clear effect between cognitive performance and B vitamins either alone or combination.

Keywords: *B vitamins, folate, B6, B 12, cognitive function, AD*

1. Introduction

A Cognitive impairment is one of global issues which is more prevalent clearly in elderly community. It is defined as declination of cognitive function related to age and neurological conditions (Pau´ l et al., 2009) which may include forgetfulness, learning difficulty, loss of higher reasoning, inability to concentrate, as well as low intelligence and mental functions. Furthermore, cognitive decline is linked closely with dementia and Alzheimer disease (AD) in long term. So, In the worldwide approximately 37 million people have suffered from dementia in 2010, and this number will be increased during 20 years coming to be in 2030 approximately 65 million and around 115 million in 2050 (World Alzheimer Report. 2009; WHO, 2012). The timing of onset of the cognitive decline is still Controversies (Salthouse. 2009; Hitt., 2012; Singh-Manoux et al., 2012; Plassman, et al., 1995). Thus, a lot of studies try to discover the preclinical stages before onset of the clinical signs of advanced cognitive decline such as dementia and then to AD to find protection treatment (Jone S. 2005; Sperlinga et al., 2011; Rentz et al., 2004; Pau´ l et al., 2009). Holford (2011) stated that the clinical manifestation of brain shrinkage and memory dysfunction appears in period of 30 to 40 years (Holford. 2011).

Thus, many in vitro and in vivo studies indicated to the role of such nutrients to enhance the brain function by acting in variety of processes involved in neuronal function and the synthesis of neurotransmitters. The nutrients that are considered important for cognitive function are: B vitamins particular(B6, B12, folate) and flavonoids.

2. B Vitamins and Cognitive decline

B vitamins are soluble in water, as well as, body cannot synthesize these vitamins. So, the dietary intake and supplementation of these vitamins for all ages are important to achieve the optimum cognitive health and to prevent the change in the brain function as many studies proven that. As well as, the main source of B12 are dairy products, eggs, poultry, meat, and fortified food. Likewise, B6 are beans, legumes, cereal, meat, and nuts. Also, some studies have shown the important role of folate in central nervosa system (CNS) which exists in dark green vegetables, beans, Orange Juice and fortified grains and cereals to obtain enough folate (Meschino. 2002). The average intakes of B vitamins as according to the Dietary Reference Intakes (DRIs) are clarified in table 1.

Table 1:Dietary Reference Intakes (DRIs) for male and female:

	Male		Female	
	31-50y	51-> 70y	31-50y	51->70 y
Folic acid (mcg)	400	400	400	400
Vitamin B6 (mg)	3.1	1.7	3.1	1.5
Vitamin B12 (mcg)	2.4	2.4	2.4	2.4

In addition, studies are growing which suggest that the adequate of dietary intake of B vitamins might be able to protect and delay the decline which will happen on the cognition, which means that optimal B vitamins status in the blood can enhance memory performance and other mental capacity. Moreover, they are playing an essential role in CNS function by synthesis of neurotransmitters, engaging in the neuropathology and neuropsychiatric syndromes such as dementia, depression or mood disorder, and AD (Meschino. 2002; Reynolds, 2006). Thus, the deficiency of these vitamins affects homocysteine (Hcy) level which is associated with higher incidence of cognitive impairment, and brain atrophy (Tani et al., 2008; Clarke et al., 1998). So, Hcy level regulated by B-vitamins (folate or B9, vitamins B-6 and B-12) and any deficiency of these vitamin causes increase of Hcy level in the plasma which also called hyper-homocysteinemia (HHcy). HHcy is associated with ageing, cerebrovascular disease, stroke and several neurodegenerative and psychiatric disorders which include depression, AD and Parkinson's disease (PD) (Stanger et al., 2009; Van Dam et al., 2009; Graham et al.,1997).

As well as, a study which demonstrates the important role of folate, vitamin B6, and B12, found the deficiency of these nutrients in mouse model of AD, i.e. Tg2576, led to HHcy and increased accumulate of Amyloid beta (Ab) levels in the cortex and hippocampus (Min Zhuo & Praticò. 2010). The link between B vitamins and cognitive performance are involving in their capability to regulate homocysteine plasma level and prevent vascular dementia and cerebrovascular disease, that by engaging in homocysteine methionine metabolism, synthesis of neurotransmitter, and works as methyl donor (Chacon et al., 2009; Stanger et al., 2009). Thereby, dietary intake of these vitamins could be helped to monitor the Hcy level and prevent the cognitive decline.

1. Homocysteine and Cognitive function

Homocysteine (Hcy) is considered as a sulfur-containing amino acid produced as a result of metabolism of amino acid (methionine) (Sachdev, 2004). HHcy is an independent risk factor for vascular disease, cognitive impairment, AD, and neuropsychiatric disorder (Ling Fuh. 2010; Stanger et al., 2009; Van Dam et al., 2009; Graham et al., 1997). The mechanisms of the effects of Hcy on cognitive function remain controversial. Thus, the HHcy may contribute to develop the cognitive decline or vascular dementia by the development of cerebrovascular endothelial dysfunction, DNA hypo-methylation, oxidative stress, as well as increase accumulate of beta amyloid neurotoxicity, and neuronal apoptosis.

According to plenty of studies which explained the metabolisms of Hcy which could be described in two pathways which are; re-methylation pathway which requires folate and B12 as coenzymes and trans-sulfuration pathway which requires B6 (pyridoxal-5'-phosphate) as a coenzyme. Thus, B vitamins help to complete the metabolism of Hcy to convert homocysteine to methionine after forming of S-adenosylmethionine (SAM), so that requires B-12 and folate as co- factor. SAM is important for biological methylation reactions that by donating a methyl group (CH3) which helps to convert SAM to S-adenosylhomocysteine (SAH). SAH subsequently forms to homocysteine. In normal case 50% of Hcy is a methylation and another 50% is a trans-sulfuration to cysteine, and the last reaction requires vitamin B6 as a co-factor. Then the product of trans-sulfuration (cysteine) uses to make glutathione which considered as an antioxidant which work to protect cells from oxidative damage (Finkelstein et al., 2000; Mudd et al., 2001; Sorina Cătană et. al., 2011).

So, the deficiency of B vitamins acts to increase concentration of cellular SAH in endothelial cells which lead to DNA hypo-methylation because SAH acts as an inhibitor of DNA methyltransferase (Dnmt) activity (Davis and Uthus. 2003; Sibani et al., 2002; Lee and Zhu. 2006). Also, that might cause changing in gene expression and then subsequently neuron death. Therefore, elevated Hcy leads to neurotoxicity which might be described as a DNA damage then apoptosis (Jamaluddin et al., 2007). However, there is a strong association between the pathology for both of the cerebrovascular and Alzheimer's disease through the appearance of the early clinical signs of dementia or cognitive decline (Ling Fuh, 2010). This is very evident through the role of Hcy, where HHcy inhibits the endothelial cells growth as well as may cause vascular injury or damage in the lining of the arteries and may make blood clot (thrombus), which leads to increase the risk of blood vessel blockages. When the thrombus move by bloodstream to brain lead to stroke. Stroke induces cognitive decline. Thus, the cognitive decline may occur as threefold for those who had experience with stroke. Also, about 25% of these cases developed to dementia (Khedr et al., 2009; Ling Fuh. 2010; Danovska et al., 2012).

Additionally, Glutamate transporters or excitatory amino-acid transporters (EAATs) act on the extracellular to remove glutamate which eliminates the excitatory signal in neuronal synapse into neuroglia and neurons. In case of HHcy which leads to stroke, brain injury, and neurodegenerative disease glutamate build up on the extracellular neuron cells which influence the NMDA receptors (N-methyl-D-aspartate) channels function then allow to the calcium ions to access inside the cells, thereby neuronal damage. In addition, the excessive intracellular of Ca2+ ions lead to mitochondria damage and this mechanism is called excitotoxicity. Also, a cerebral mitochondrial dysfunction is contributing to produce oxidative stress which considered as an attribute for some neurodegenerative disease such as AD, PD (Fiskum et al., 1999; Shukla et al., 2011).

2. Supporting evidence for nutritional effect on Hcy

Several studies demonstrate the effect roles of B vitamins on cognitive function particularly memory and nonverbal thinking which influence by the deficiency of these vitamins (Goodwin et al., 1983). Thus, there are many studies which focused on this field whether in vivo or in vitro.

However, the role of B vitamins is essential for methylation capacity, where they play an important role in the liver to confer the phosphatidylethanolamine (PE) to phosphatidylcholine (PC) by PE-N-methyltransferase (PEMT), as reported in several studies the role of PEMT to transfer polyunsaturated fatty acids (PUFAs) such as DHA or docosahexaenoic acid from liver to plasma then tissues that need to B vitamins to enhance PEMT activity to synthesis PC. (VanWijk et al., 2012; Yamamoto et al., 1987). As well as, DHA is essential for learning ability. A further study which conducted by Soderberg et al (1991) found that people with AD had the low level of DHA in the hippocampus compared with the same age samples brain of the control group (Hashimoto et al., 2005). That which may reverse the essential role of B vitamins.

Additionally, Smith et al (2010) found that B vitamins have a dramatic role to slow the rate of brain atrophy in older people with Mild Cognitive Impairment (MCI) after treating them for over 2 years with B vitamins supplementation (B6, B12, B9), as well as, the extended study of Smith's study found that these vitamins help to slow cognitive decline and clinical signs particularly for people who have high level of Hcy in the baseline (Smith et al., 2010; de Jager et al ., 2012). So, found 67% of elder people with HHcy (>14 μmol/L) have a low plasma concentration of B vitamins which is insufficient to biological reaction (Selhub et al., 1993). Also, Tani et al (2008) has been stated that a long-term of dietary intake of vitamin B6 may be associated with lower incidence of cognitive impairment in the elderly people because it is related to decrease Hcy level. However, Ubbink et al (1995) found no effect of B6 on plasma Hcy, While B12 and folic acid showed the significant effect by lowering Hcy level. Likewise, a study which documented the lack of significant relationship between the fasting

plasma Hcy and vitamin B6 in animals and humans after administration with diet which contains vitamin B6 deficiency (Miller et al . 1992).

In addition, further evidence from a systematic review of fourteen randomized trials suggested that there are no sufficient evidences for a useful effect of vitamins B6, and B12 and folic acid supplementation alone or combination alike in population level on cognitive ability for people who have either normal or cognitive deficit (Balk et al., 2007). In a double-blind placebo-controlled trail documented that oral supplementation of B12 vitamin alone or combination with folic acid did not improve cognitive performance in old people with mild vitamin B12 deficiency after treated them for 6 months, but it was able to correct the deficiency (Eussen et al.,2006). Likewise, a study for short period (3 months) suggested that treatment with vitamin B12 did not enhance the cognitive ability and symptoms of depression in short term (Hvas et al., 2003). Additionally, a recent study which conducted by McNeill et al (2011) in Edinburgh Scotland, UK. This study consisted of survey for 1091 men and women who were born in 1936 and they had a measurement of intelligence quotient (IQ) in age 11 years. Then at age 70, the measurement of cognitive performance had been done by a variety of cognitive tests battery, as well as completed semi-quantitative food-frequency questionnaire (FFQ). This study concluded that no relationship between dietary intake of B vitamins and antioxidants on cognitive performance at later life (McNeill et al., 2011).

However, a long-term randomized placebo-controlled study which was conducted by Kang et al (2008) on women with high risk of CVD and the role of B vitamin supplementation on cognitive function. They found B supplementation did not help to delay the cognitive decline among those women, and they did not observe any benefits after treating them with B vitamins supplementation. While, they noticed some benefits of B supplementation on cognitive performance at baseline among the women with a low dietary intake of the B vitamins.

3. Conclusion

Although the essential biological roles of B vitamins on health and cognitive function, there were conflicting evidence about the effect of B vitamins on cognitive performance and that may return for many factors like changes in digestive system related to age, as well as, some drugs which affect the absorption of these vitamins. Also, B vitamins supplementation along with dietary intake of vitamins B could help to obtain the sufficient intake of B vitamins. The association between long term dietary intake of B vitamins and cognitive impairment in elderly people needs more investigation.

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