any conditions. The lithium effects on HSP upregulation might be caused by the inhibition of glycogen synthase kinase-3 [2] which was suggested to be the most critical mediator of lithium functions [3] rather an increase of brain temperature. Further, Ref. [4] in Salerian et al. [1] should be the paper published on PNAS [3] rather Mol Neurobiol Sect as the authors cited.

Secondly, the measurement of body temperature does not necessarily reflect the brain temperature, which is controlled precisely during normal brain activities. Thus the effects of low environment temperature on brain activities may largely attributed to the altered blood circulation rather a changed and lower brain temperature, implying an indirect mechanism. Moreover, depression can reflect both the down-regulation of physical activities and the recurrence of depressive thoughts in the brain, namely, increased brain activity rather the down-regulation of it. These point out that brains in patients of depression might be as active as the people with mania, thus we should differentiate the brain activity with mood states.

Additionally, though cold weathers were sometimes linked with depressive thoughts, it has been suggested exposure to cold can activate the sympathetic nervous system and regulate neurotransmitter levels in blood, thus can even be antidepressive [4]. This indicates that the controlled state of hyperthermia might be helpful in treatments to depression rather causing it.

Last but not least, the modulation of brain temperature might affect functions that are critical for life activities. Currently there is no approach that can alter the temperature of specific brain area without causing side-effects on others.

Collectively, the therapeutic value of controlling mood by modulation of brain temperatures was largely weakened.

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Metabolic syndrome: A potential culprit for Alzheimer's disease?

The etiology of Alzheimer's disease has been mysterious for more than a century, clearly Alzheimer's disease falls into the incomprehensible class [1]. Recently, emerging evidence suggests that components (including hyperglycemia, hypertriglyceridemia, and a low HDL cholesterol concentration) of the Metabolic syndrome (MS) either in isolation or in aggregate may impact the onset or severity of neurodegenerative processes, including those physiologic changes that lead to Alzheimer's disease (AD) [2,3]. Epidemiology studies also revealed that the incidence of AD was increased significantly in MS patients as compared with normal controls. However, the mechanisms through which the metabolic syndrome and its components may be associated with Alzheimer disease remain elusive.

Hyperglycemia, a marker for insulin resistance, have been implicated in the association between MS and AD [3,4]. Intake of sucrose-sweetened

water exacerbates memory deficits and amyloidosis in a transgenic mouse model of Alzheimer's disease [5]. One possible reason might be the direct effect of insulin resistance on the brain. Insulin can influence the insulin level in the brain, and modulate the aggregation of β-amyloid protein, which are one of the more specific diagnostic and neuropathologic markers of AD [3]. In addition, insulin can inhibits the activity of glycogen synthase kinase-3 enzyme, prevents the tau hyperphosphorylation and induces inflammation through distinct mechanisms [6,7]. Another possible culprit is the low plasma triglycerides and HDL cholesterol, which are also one of the components of MS. HDL cholesterol is the main transporter of cholesterol in the brain, and a reduction in the HDL cholesterol concentration may result in the impairment of cholesterol release to neurons, which further lead to the formation of neurofibrillary tangles and senile plaques [7,8]. In addition, a high plasma triglyceride concentration and a low plasma HDL concentration are well established risk factors for atherosclerosis and could at least partly explain the vascular changes in the brains of patients with AD [3]. In animal models, it is also clear that experimental dietary hypercholesterolemia exacerbates amyloid deposition, whereas pharmacological reduction of cholesterol reduces amyloid burden [9]. In humans, reduction of plasma cholesterol levels with statins has also been reported to significantly reduce AD prevalence [10].

Taken together, these data strongly indicate that Alzheimer's disease is associated with metabolic syndrome, mainly due to insulin resistance, hyperinsulinemia and abnormal peripheral lipid metabolism. Therefore, life style intervention, such as rational diet and proper physical activity, which have been shown to reduce the risk of the metabolic syndrome, could have a role in the prevention and treatment of Alzheimer's disease. However, further studies to confirm this belief are awaited.

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