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The effect of education on regional brain metabolism and its functional connectivity in an aged population utilizing positron emission tomography

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ABSTRACT

Education involves learning new information and acquiring cognitive skills. These require various cognitive processes including learning, memory, and language. Since cognitive processes activate associated brain areas, we proposed that the brains of elderly people with longer education periods would show traces of repeated activation as increased synaptic connectivity and capillary in brain areas involved in learning, memory, and language. Utilizing positron emission topography (PET), this study examined the effect of education in the human brain utilizing the regional cerebral glucose metabolism rates (rCMRglcs). 26 elderly women with high-level education (HEG) and 26 with low-level education (LEG) were compared with regard to their regional brain activation and association between the regions. Further, graphical theoretical analysis using rCMRglcs was applied to examine differences in the functional network properties of the brain. The results showed that the HEG had higher rCMRglc in the ventral cerebral regions that are mainly involved in memory, language, and neurogenesis, while the LEG had higher rCMRglc in apical areas of the cerebrum mainly involved in motor and somatosensory functions. Functional connectivity investigated with graph theoretical analysis illustrated that the brain of the HEG compared to those of the LEG were overall more efficient, more resilient, and characterized by small-worldness. This may be one of the brain's mechanisms mediating the reserve effects found in people with higher education.

1. Introduction

Education in schools involves systematic learning in an environment conducive to learning new information and academic skills. It involves repetitive learning of various cognitive functions and skills such as memory, language, mathematics, and logic. This process usually takes place from childhood to early adulthood when brain plasticity is the greatest. On the other hand, training involves specific physical or mental repetitive learning aimed at improving one's capability, productivity and performance (Neubauer and Fink, 2009; Ericsson and Ward, 2007). Physical or job training is usually narrower in extent and shorter in duration compared to school education. Learning, whether by training or school education, is a process that modifies the brain through experiences. Therefore, it can be postulated that school education will result in changes in the broader brain regions involved in memory, language, mathematics, and logic. However, training will likely be followed by change in a limited brain region involved in the specific skill or job that was trained.

Numerous studies have investigated how experiences an animal has modify its brain. Diamond and her colleagues (1988) were one of the first teams to find experimental evidence where experience changes the brain at various levels. They analyzed the brains of rats bred in enriched environments (EE) and those bred in impoverished environments (IE) over many years. The results showed that there were differences in the thickness of the cortex, the size of the

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pyramidal cell body, the length and number of dendritic branches, the number and contact areas of the synapses, and the number of glial cells between the two conditions in many regions of the rat brain. Although the trend decreased with age, it nonetheless continued. Similarly, Sirevaag and Greenough (1987) found that rats in complex environments had a greater number of synapses per neuron compared to those in isolated environments. They also had increased metabolism such as larger capillary volume per neuron and larger mitochondria volume per neuron in the occipital cortex. More recent studies examined the effects of motor training on the brain and found that it increased the number of postsynaptic dendritic spines over time in the mouse cortex and left minute, but more permanent marks like lifelong surviving spines and synapses (Yang et al., 2009; Xu et al., 2009).

Although sparse, studies on humans had similar findings regarding training or EE on the brain. A selective increase in brain gray matter was reported in elderly people after motor training (Boyke et al., 2008; Draganski et al., 2004). Other studies examined the effect of training on expert performance. For example, a well-known London Taxi driver study showed how extensive training in the spatial memory function was associated with increased hippocampus size in the drivers (Woollett and Maguire, 2011). Additionally, a comparison of professional musicians with amateur musicians and non-musicians showed differences in gray matter volume in motor, auditory, and visual–spatial brain regions (Gaser and Schlaug, 2003).

Furthermore, studies (Haier et al., 1988, 1992a, 1992b; Parks et al., 1988) examining the relationship between training and absolute cerebral glucose metabolic rates quantified with PET and 18-fluoro-2-deoxyglucose (FDG) have shown a significant decrease in whole brain glucose metabolism after learning. This supported the efficiency hypothesis (Haier et al., 1988), which states that the brains of those who are better at a task are more efficient (i.e. use less energy performing the task). However, studies investigating the effects of education on the brain have been sparse. One experimental study found that during auditory sustained attention tasks, people with longer period of education had relatively higher glucose metabolism in the left posterior cingulate gyrus, the left precuneus, and bilateral lingual gyri in a small sample of adult subjects (Eisenberg et al., 2005).

An indirect support for the effect of education on the human brain comes from clinical studies that report longer delays in dementia manifestation in patients with higher education (Bennett et al., 2003; Roe et al., 2007; Garibotto et al., 2008; Stern, 2002). This hypothesis is supported by neuropathologic studies that show variability in the relationship between the severity of brain pathology and clinical manifestations (Garibotto et al., 2008). This is consistent with animal experiments where enhanced learning (multiple learning sessions or relatively strong stimulation) had protective effects against amnestic treatments regardless of the task, reinforcement type, animal type, and the agent causing amnesia (Rodriguez-Ortiz and Bermudez-Rattoni, 2007; Prado-Alcalá et al., 1972, 1978, 1980; Prado-Alcalá and Cobos-Zapiaín, 1977, 1979; Quiroz et al., 2003). Enhanced learning by humans is likely to take the form of longer education or training in broader sense that may involve job or expertise. Consequently, it might be similar to the results found in animal studies. The cognitive reserve effect observed in the highly educated elderly population (Coffey et al., 1999; Stern, 2002; Hanyu et al., 2008) is consistent with the results of enhanced learning. Even though, cognitive reserve has been studied extensively to elucidate the role of education in dementia development, no study, to our knowledge, has examined the direct effects of extensive education on the senescent brain.

Education involves repetitive learning of a variety of cognitive skills and knowledge. These acquired skills and knowledge, developed from extensive education, are likely to construct new, intensive, efficient, and stable (resilient and robust) neural networks that mediate cognitive functions like memory, language, and higher-cognitive processes. Such skills and knowledge appear to inhibit inefficient networks while enhancing efficient ones in order to save resources during tasks (Haier et al., 1992a, 1992b). Since more intensive and efficient networks would consist of connections with larger diameters and more synapses with more vessels in the vicinity, significantly more energy will be required by the network in the resting state. Therefore, we hypothesized that the elderly with high-level education would have increased glucose metabolism in brain regions associated with memory, language, and higher-cognitive processes than those with low-level education. In addition, functional connectivity among the regions was hypothesized to be more efficient and resilient in the highly educated elderly population.

Utilizing graph theoretical analysis methods, important topological parameters of the brain network like small-worldness, global efficiency, network resilience, and the hubs or highly connected regions as well as the local network parameters were examined. Small-worldness is a feature characterized by high clustering with short path lengths between nodes (Watts and Strogatz, 1998). Global efficiency is an indicator of parallel information transfer in the network (Achard and Bullmore, 2007) while network resilience is an indicator of responses to random failure and targeted attack. The hub is an important regulator of information that has high centrality, interacts with many other regions, facilitates functional integration, and plays a key role in network resilience to insults.

The purpose of the current study was to examine the effect of education on regional glucose metabolism and its functional connectivity in the human brain, both based on the principle of synaptic plasticity, which would predict that long-term education would change the brain regions involved in cognitive skills and knowledge even in senescence. Using PET, we first compared the regional glucose metabolic rates (rCMRglcs) of elderly women with high-level education (henceforth HEG) and those with low-level education (henceforth LEG) in the resting state by using the region of interest (ROI) analysis to compare the rCMRglc between the two groups. A graph theoretical analysis using the rCMRglcs computed from ROI analysis examined differences in the functional network properties of the two education groups.

2. Participants and methods

2.1. Participants

Participants consisted of women between the ages of 61 and 85 who registered for a recreation and culture course at a senior program operated by a church in Gangnamgu, Seoul from 2004 to 2008. These women participated in the Seoul Aging Study, which involves dementia evaluations using the Korean-Dementia Rating Scale (K-DRS; Chey, 2006) and the Elderly Memory Disorder Scale (EMS; Chey, 2007) that assesses overall cognitive functioning and memory, respectively. Additionally, semi-structured interviews and questionnaires were conducted to measure daily cognitive and behavioral functioning. Subjects were deemed normal and not demented based on the two neuropsychological tests as well as interviews and questionnaires. Individuals with head trauma history and any clinical neuropathology as well as left-handed or ambidextrous individuals were excluded from the analysis. Those who had physical conditions known to compromise cognitive capacity (such as hypertension or uncontrollable diabetes) were excluded as well. Only 85 out of the 105 subjects passed the aforementioned criteria. Within this sample, we were able to define two groups of elderly women with respect to their education