Chapter 39
Diabetes-Related Cognitive Decline, a Global Health Issue, and New Treatment Approaches

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ABSTRACT

The epidemic of type 2 diabetes (T2DM) is spreading around the globe and challenging the unprecedented success of health sciences in increasing longevity. T2DM has been linked to accelerated brain aging, functional decline in older adults and dementia. Brain insulin resistance and glycemic variability are potential mechanisms underlying T2DM-related brain damage and cognitive decline. Intranasal insulin therapy has emerged as a potential new treatment for T2DM-related cognitive impairment. Wearable technologies now allow better monitoring of behaviors and glycemic levels over several days and deliver real time feedback that can be used to improve self-management and lead to new prevention strategies and therapies for T2DM complications.

DOI: 10.4018/978-1-5225-5484-4.ch039

INTRODUCTION

Healthcare sciences have achieved an unprecedented success in continuing increase in longevity, decrease of birth death rates and diminishing or eliminating the impact of many infectious diseases. Large health inequalities between countries around the globe shape differences in lifespan from < 50 to > 80 years of age. At the same time, non-communicable diseases, and in particular diabetes, hypertension and cardiovascular diseases have become the most common causes of death. Over the last twenty years, the obesity epidemic has been sweeping across the globe, and many countries face a dilemma of fighting both hunger and obesity at the same time. Type 2 diabetes mellitus (T2DM) is a complex metabolic disease that affects multiple organ systems and interactions among them (Figure 1). T2DM accelerates brain aging (Mogi & Horiuchi, 2011; Xu, Qiu, Wahlin, Winblad, & Fratiglioni, 2004), alters neurovascular coupling (Cersosimo & DeFronzo, 2006; Chung et al., 2015; Tiehuis et al., 2008), and increases the risk for dementia and Alzheimer's disease (de Bresser et al., 2010; van den Berg et al., 2010). Long-term impact of T2DM on cerebral vasculature further contributes to high prevalence of cognitive impairment, depression, and disability in older adults (Saczynski et al., 2008). Memory loss further deteriorates self-care and glycemic control and accelerates disease progression, worsening a vicious cycle of functional decline. Most recent research emphasized the role of brain insulin in neurotrophic signaling, neuromodulation, nutrient homeostasis and metabolism. A new concept of brain insulin resistance has emerged, as potential pathways for altered transport and signaling within the brain, as well as between the brain and the periphery, as a potential mechanism underlying DM-related cognitive decline.

Currently, there is no cure for DM-related cognitive impairment. Therefore, there is an urgent need to develop new therapies to target insulin delivery to the brain to treat cognitive impairment in older diabetic adults. In this paper we review the pathophysiology of insulin action within the brain, as well as

Figure 1. T2DM–a complex multi-organ disease