A nuclear receptor expressed in the adrenal glands, gonads, anterior pituitary, and ventromedial hypothalamus nucleus (VMH) is steroidogenic factor 1 (SF-1) [1]. Not only for the production of VMH, but also for its physiological functions, SF-1 is essential [2]. The VMH is a significant hypothalamic nucleus that is important for controlling feeding and preserving homeostasis of whole body resources. VMH lesions change feeding habits and are associated with hyperphagia and obesity development [3]. Likewise, VMH acts as a nutrient sensor and has been shown to respond to decreasing nutritional conditions such as hypoglycemia by inhibiting the development of insulin and by stimulating the release of glucagon and catecholamines [4]. The expression of leptin receptors in the VMH also indicates the importance of this nucleus in reacting to leptin-induced feeding, metabolism and control of energy balance [2].

Increasing public health issues are metabolic complications such as obesity, diabetes, and insulin resistance, and their incidences are increasingly increasing. Glucose and insulin homeostasis imbalances in the whole body are also closely related to the pattern of increased obesity. Thus it is important for the creation of new strategies for prevention and treatment of metabolic syndromes, including obesity and diabetes, to know the molecular and cellular processes underlying energy balance, glucose and insulin homeostasis. The hypothalamus, especially the medium-basal hypothalamus, has been viewed as a site for homeostatic control of the entire body, including body weight and energy metabolism. While classical approaches have significantly expanded our understanding of the physiological roles of medium-basal hypothalamic areas, such as electronic/chemical lesioning or microinjection of a compound into a specific site. For example, VMH electronic/chemical damage is likely to affect the nearby areas or the descending fibers that pass through the VMH [5]. Moreover the microinjection into the hypothalamic site of any compounds is vulnerable to off-target effects (e.g. leakage of compounds beyond the intended site). The creation of new modern biotechnology at the levels of specific neurotransmitter systems, particularly genetic manipulation techniques, will allow us to resolve these caveats and provide an advanced chance to explore the neurological functionality comprising the energy balance mechanism in a particular hypothalamic nucleus.

As essential metabolic regulators in the VMH, previous studies have involved SF-1 and SF-1 neurons [6-8]. However the whole body SF-1 knockout is fatal attributed to adrenal insufficiency, corticosterone injection and adrenal transplants save the SF-1 knockout mice, but are followed by extreme obesity, suggesting that SF-1 dysfunction changes the metabolism of energy [9]. Mice without SF-1 leptin receptor releasing neurons directly in the VMH displayed symptoms of metabolic syndrome comprising obesity, elevated levels of insulin and leptin and reduced resistance to glucose [2,10]. In addition, in SF-1 neurons, insulin receptor knockout mice displayed enhanced glucose metabolism and were preserved from high fat diet-induced leptin resistance and weight gain and elimination of the transcription factor FoxO1 in SF-1 neurons, showing increased energy consumption and better insulin sensitivity with an overall lean phenotype [11]. In particular, for a normal counterregulatory response to hypoglycemia, the glucose-sensing ability of VMH glucose-inhibited neurons is not needed. Instead in the event of impaired hypoglycemia detection by peripherally located glucose detection systems that are linked to the VMH, it can represent a fail-safe device [12]. Whereas these studies point to the significance of SF-1 neurons in preserving normal...
Steroidogenic Factor 1 (SF-1) as Important Metabolic Regulators in the Ventromedial Nucleus of the Hypothalamus (Vmh)

energy homeostasis in the VMH, the mechanism by which SF-1 regulates this energy metabolism is not really described. Furthermore the function of SF-1 was not well explicated in modifying age-dependent energy homeostasis within various nutritional situations.

Genetic tests have also illustrated that SF-1 neurons are essential parts of the system assumptions underlying glucose homeostasis, in addition to the significant role of SF-1 neurons in controlling energy homeostasis. The AMP-activated protein kinase (AMPK) VMH energy sensor maintains glucostasis through neurotransmitter signals that decrease [γ-aminobutyric acid] or increase counter-regulation of [nitric oxide] [13]. VMH ‘fuel-inhibited’ neurons are responsive to the metabolic substrate stream produced by astrocytes [13]. Norepinephrine (NE) controls the in vitro metabolism of astrocyte glycogen and hypoglycemia intensifies the activity of VMN NE In vivo [13]. Distinguishing NE effects on the expression of VMN astrocyte adrenergic and estrogen receptor variants indicate that noradrenergic glycogen metabolism control can be regulated, in part, by one or more receptors defined by catecholamine sensitivity [13]. The association between VMH glycogen augmentation and attenuated hypoglycemic VMH gluco-regulatory neuron AMPK activity indicates that during this metabolic hazard, the expansion of this fuel reservoir maintains cellular energy stability [14]. However, it showed that VMH-specific deletion of SF-1 blunts (a) the reductions in fat mass, (b) improvements in glycemia, and (c) increases in energy expenditure that are associated with exercise training [15]. Another, it has found that SF-1 deletion in the VMH attenuates metabolic responses of skeletal muscle to exercise, suggesting that SF-1 expression in VMH neurons is required for the beneficial effects of exercise on metabolism [15].

In conclusion, several genetic approach suggests that SF-1 neurons of the VMH are a crucial subset of neurons that play a significant role in brain hypoglycemia counterregulation. Therefore, future research analyzing these complex networks would not only be beneficial in understanding brain-regulated glycemic homeostasis, but also in promoting the development of drugs to potentially treat diabetes.

Bibliography


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