Type 2 diabetes disturbs Kir4.1 rhythm in retinal Müller cells

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The Müller cells function as a principal glia of the retina and maintain water homeostasis and K^+ concentration via the specialized inwardly rectifying K^+ (Kir) channels. About six to seven Kir channels have been found, among which Kir4.1 is expressed abundantly in Müller cells. Diabetes leads to a decrease in Kir4.1 expression and of potassium currents. For this study, we hypothesized that a diurnal change in Müller cell metabolism plays an important role in regulating the Kir4.1 expression. We tested our hypothesis using an animal model of type 2 diabetes (T2D;db/db mice) and in an *in vitro* study on the rat Müller (rMC-1) cells. The electroretinogram (ERG) assessment was performed on db/db mice to evaluate the Müller cell dysfunction. The rhythm of protein expression of Kir4.1 was examined in rMC-1 cells by western blot. The 'b' wave of an ERG, a characteristic of K^+ ion distribution across the retina exhibited a diurnal rhythm in a mouse retina. The oscillatory pattern of ERG response was profoundly dampened in db/db mice. The clock synchronized rMC-1 cells *in vitro* exhibited a consistent oscillatory pattern for clock genes. The Kir4.1 protein in rMC-1 cells showed a regular pattern of the peak and troughs, consistent with the functional cock. Our studies suggest that Kir4.1 channels possess a diurnal rhythm and with T2D this rhythm is dampened.