potentially detrimental increase in grid scale in the same mouse strain. It is possible that HCN1 knockout aids learning by increasing the spatial stability of grid cells and border cells, leading to a more stable representation of the environment. This increase in spatial stability could result from the well-documented enhancement of long-term potentiation observed with HCN1 knockout (Nolan et al., 2004; Tsay et al., 2007).

DISCUSSION

The topographical organization of the grid cell network can be characterized by the slope of the dorsal-ventral gradient in grid spacing (slope), as well as the Y intercept of that gradient (ΔY). With loss of HCN1, we found a significant increase in the Y intercept, indicating that the electrophysiological properties of single neurons can strongly influence the scale of spatial representation. The increase in grid scale was accompanied by an increase in the interspike interval of theta modulated grid cells, suggesting that grid scale and theta frequency are mechanistically related. In contrast to the global shift in grid scale (ΔY), the steepness of the gradient (slope) remained unaffected. There was also no change in the theta period of entorhinal interneurons or in the proportion or properties of head direction cells and border cells.

The selective change in the Y intercept (ΔY) constrains the number of potential cellular mechanisms that could contribute to grid scale. Reducing Ih by knockout of HCN1 or pharmacological manipulation has differential effects on resonant and temporal-integrative gradients of entorhinal cells recorded in vitro (Figure S5). Knockout of HCN1 results in profound flattening of the dorsal-ventral gradient in resonance (Giocomo and Hasselmo, 2009), suggesting that the slope of that gradient depends almost exclusively on a gradient in the h current. The lack of a corresponding change in the slope of the gradient in grid scale indicates that the topographical expansion is not determined by HCN1-dependent resonance (Dodson et al., 2011). This has potential implications for a class of computational models termed “oscillatory interference models” (Blair et al., 2008; Burgess et al., 2007; Giocomo et al., 2007; O’Keefe and Burgess, 2005) in which the change in grid scale is generated by variations in the resonant frequency along the dorsal-ventral axis (Burgess, 2008; Giocomo et al., 2007; N. Burgess et al., 2005, Computational Cognitive Neuroscience, conference). The reduction in modulation of theta frequency by running speed seen with the loss of HCN1 is consistent with predictions made by some of these models (Burgess, 2008; Burgess et al., 2007). However, the pronouncedly slower oscillation observed...