Spatiotemporal regulation of multiple overlapping sense and novel natural antisense transcripts at the nrgn and camk2n1 gene loci during mouse cerebral corticogenesis.

ABSTRACT

Nrgn and Camk2n1 are highly expressed in the brain and play an important role in synaptic long-term potentiation via regulation of Ca 2 +/calmodulin-dependent protein kinase II. We have shown that the gene loci for these 2 proteins are actively transcribed in the adult cerebral cortex and feature multiple overlapping transcripts in both the sense and antisense orientations with alternative polyadenylation. These transcripts were upregulated in the adult compared with embryonic and P1.5 mouse cerebral cortices, and transcripts with different 3′ untranslated region lengths showed differing expression profiles. In situ hybridization (ISH) analysis revealed spatiotemporal regulation of the Nrgn and Camk2n1 sense and natural antisense transcripts (NATs) throughout cerebral corticogenesis. In addition, we also demonstrated that the expression of these transcripts was organ-specific. Both Nrgn and Camk2n1 sense and NATs were also upregulated in differentiating P19 teratocarcinoma cells. RNA fluorescent ISH analysis confirmed the capability of these NATs to form double-stranded RNA aggregates with the sense transcripts in the cytoplasm of cells obtained from the brain. We propose that the differential regulation of multiple sense and novel overlapping NATs at the Nrgn and Camk2n1 loci will increase the diversity of posttranscriptional regulation, resulting in cell- and time-specific regulation of their gene products during cerebral corticogenesis and function.

Keyword: Nrgn; Camk2n1; Noncoding RNA; Cerebral cortex; Cerebrum; P19 cells.