GABAergic signaling has widespread effects in early development.

GABAergic signaling has been shown to crucial to early circuit and excitatory synapse development. Because GABA channels are permeable to chloride, a relatively inert ion which has few known intracellular signaling effects, and which is also much less 'dangerous' to the cell in terms of excitotoxicity than Ca2+ or Na+, GABA signaling represents fairly safe regulating system during development. In addition, there is a good deal of mutability of GABA's effects based on the chloride gradient. In immature neurons, high expression of transporters like NKCC1 establish a chloride gradient which makes GABAR activation depolarizing; later these transporters decrease in number and are replaced by increases in NKCC2 and KCC2 expression, which alter the gradient making GABAR activation hyperpolarizing in adult neurons. This malleability allows GABA signaling to have different effects during different developmental time points. Extensive data has shown that GABA is depolarizing in young neurons, and that GABA signaling begins even before synaptogenesis. GABA may function as the 'switch' between signaling neuronal progenitors to proliferate and signaling such cells to fully differentiate, as it is released by neuroblasts and may in turn activate GABA receptors on neural progenitor cells (Ackerman and Cline, 2007). Furthermore, alterations in the chloride gradient have been implicated in abnormal morphological development in the dendrites and axons of cortical neurons, and perturbed ratios of inhibitory and excitatory inputs. In a recent 2008 study by Wang and Kriegstein, shRNA was used to knockdown NKCC1 in newborn cortical neurons, resulting in a chloride reversal potential in affected cells that hovered around -70mV (as apposed to the -40mV chloride reversal potential of nearby cells which were not transfected with the shRNA against NKCC1). Shown below is a figure from their 2008 paper showing this disrupted morphology in cortical neurons.

In addition, electrophysiological recordings of spontaneously evoked postsynaptic potentials show a decrease in AMPA sPSCs overall, and a shift in the ratio of excitatory/inhibitory inputs toward increased inhibition.

GABA receptor activation is thought to mediate many of its affects on early neuronal development by facilitating Ca2+ influx, either through voltage dependent channels, or through alleviating the Mg2+ block on NMDA channels. Because NMDA channels are known to be involved in a number of key glutamatergic developmental functions (including synapse formation) this may be a crucial role for early GABA signaling.

Although some of these early effects of GABA are not wholly dependent on GABAergic synapse formation, in conjunction with known affects of GABA synaptic activity in more mature neurons on regulating excitation and circuit refinement, these examples demonstrate the importance of inhibitory neurotransmission and highlight the importance of understanding GABAergic synapse development.