We undertook this study [1] because we had found that serotonin (5-HT) as well as norepinephrine and dopamine neurons were born several days prior to those cells they will eventually innervate [2]. We chose to pharmacologically manipulate the developing serotonergic system in the embryo because of the availability of a drug, p-chlorophenylanaline (pCPA) that biochemically inhibited 5-HT synthesis [3], rather than destroying nerve terminals, as with 6-OH-dopamine [4].

Following mapping of the prenatal development of the serotonergic system [5], we were able to examine the relationship of developing 5-HT nerve terminals to their embryonic target cells and reassess data from our previous pCPA study [6]. This analysis, together with a subsequent study [7], showed a strong correlation between the spatiotemporal distribution of developing 5-HT axons, inhibition of 5-HT synthesis within these cells [7], and delayed onset of neuronal differentiation in specific regions of the embryonic rat brain [6].

Since this time, many studies have provided evidence that 5-HT acts as an important differentiation and growth regulatory signal that plays key roles in the development of the nervous system [8] as well as nonneural tissues [9]. These roles are mediated by the same receptors and second messengers utilized in neurotransmission [10], but in developing tissues, including the CNS [11, 12], gut, heart and craniofacial region [9, 13–18], ongoing ontogenetic processes allow these signals to act like growth, trophic and morphogenetic signals.


