year in the neuropeptide substance P in the human brain (Chigr et al., 1991). One can hypothesize that in humans like in experimental animals, this tendency in decreasing density may be an important step in the maturation of hypothalamic structures as has been shown previously (Sarrieau et al., 1994; Swaab, 1995). However, to establish this concept, further ontogenetic analysis of the development of the human DSIP neuronal system is needed. Although the relative regional distribution of DSIP immunoreactivity could vary in the postnatal period studied, our sample size is too small to draw definitive conclusions about developmental postnatal changes.

Our study shows variations in the immunoreactivity of DSIP in several hypothalamic structures; this, however, does not necessarily need to be related to the developmental process. The variations in hypothalamic DSIP density during the first postnatal year could be assigned to various other causes. Indeed, many patient-related factors that are non-existent in animal experiments may complicate the use of human material in such investigations (Swaab and Uylings, 1988). This kind of developmental post-mortem studies of tissues from human controls could be bedeviled by many factors of variability, due to difficulties in finding appropriate age cases and to post-mortem alterations of biochemical parameters (Denoroy et al., 1987). Although they were devoid of neurological disorders, one cannot completely rule out the possibility that their premortal status did influence the peptide amount which has been measured, and may explain all or certain changes occurring in the density of DSIP in this study. Furthermore, as human beings were not free from seasonal influences (Swaab, 1997), the time of death should be regarded as a possible factor that explains the individual variations observed in the present data. The influence of nutritional factors or drug treatment on peptidergic systems in humans has not been, to our knowledge, well taken into account (Kopp et al., 1992). Such factors should not be underestimated, especially in the hypothalamus (this part of the brain is highly implicated in the control of satiety; some side effects of drug treatments are of the neuroendocrine type).

Another factor of considerable importance in the analysis of human brain tissue is the post-mortem delay (pmd). The time between death and fixation of the brain tissue has received attention mainly from a neurochemical standpoint. Although immunohistochemical procedures for peptides are generally much less sensitive to pmd than other investigations (Bouras et al., 1986; Eymin et al., 1993), there is insufficient evidence, however, suggesting changes in the amount of DSIP present in post-mortem tissue overtime; therefore, the possibility of alteration to the nature of the peptide in the neural tissue following death cannot be totally discounted.

To our knowledge, no work has been published on possible changes related to the factors cited above in brain DSIP amounts. Our findings should be evaluated cautiously in view of the very small size of the sample we analyzed. Our preliminary study should be replicated in a large sample of newborn and infant cases dying with a wide variety of disorders, at different postnatal ages. Despite practical difficulties and obvious limitations, this is the only way to assess whether our findings are linked to sample biases and/or to introgenic artifacts or whether they reflect a neuropeptide variation underlying developmental processes occurring at this postnatal stage. Therefore, the present results have to be re-evaluated when more sample cases become available.

These studies provide evidence that DSIP immunoreactivity in several hypothalamic structures vary at different rates, and with at least two characteristic patterns. The present data represent an additional step towards the comprehension of the neurochemistry development of human hypothalamus (Bloch et al., 1984; Kopp et al., 1992; Swaab, 1995). The investigation of specific fetal stages will help us to understand the special roles of DSIP in the development of human brain. This preliminary study represents a first step towards that goal.

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