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BRAIN MRI AND OLFACTORY THRESHOLD IN THE DIFFERENTIAL DIAGNOSIS OF HYPOTHALAMIC HYPOGONADISM. P. Travaglini, T. Re, M. Farabola*, G. Broich**, C. De-Min, S. Borgato, S. Mantovani, P. Beck-Peccoz and G. Faglia. *Institute of Endocrine Sciences, and Departments of *Neuroradiology and **ENT, Ospedale Maggiore IRCCS, University of Milan, 20122-Milan, Italy.*

Anatomical, functional and genetic abnormalities may lead to dysfunction of GnRH-secreting neurons and hypothalamic hypogonadism (HH). The above neurons originate from the olfactory placode and migrate into the brain with olfactory nerves. In X-linked Kallmann syndrome (KS), mutations of a specific gene encoding for neuronal cell adhesion molecule(s) prevent cells and nerves of the olfactory placode to migrate in the brain. This results in alterations of olfactory bulbs, tracts and sulci, anosmia and hypogonadism which are characteristic of KS, but are absent in other forms of HH. In the present study, we evaluated the effectiveness of high resolution brain MRI (thin, T1-weighted and coronal sections) and olfactory threshold (standard sniff-test and diluition test) in the differential diagnosis of HH. One 44-yr-old woman with primary amenorrhea and 3 men aged 16, 42 and 47 years were studied. Basal LH [0.3±0.1 (SD) U/L] and FSH (0.7±0.2 U/L) levels were low in all patients and increased to 3-11 U/L and 2-7 U/L, respectively, in response to 3 consecutive GnRH boli (100 μg every 2 hour). Two patients (16- and 47-yr-old) complained of subjective hypoosmia and were therefore diagnosed as having KS. All had normal hypothalamic-pituitary structures and lack of obstructive disease of nasal cavities. MRI showed a normal olfactory system in all but the 16-yr-old man who had absence of olfactory bulbs, tracts and right-side sulcus. In this patient however the olfactory threshold was normal, while true hypoosmia was documented only in the 42-yr-old man with subjectively reported normal sense of smell.

In conclusion, our data highlight the current difficulties in the differential diagnosis of the various forms of HH. The discrepancies among the clinical picture, the brain MRI and the olfactory threshold recorded in the present study, point to the necessity of including in the differential diagnosis of HH also appropriate genetic studies in order to clarify the variable phenotypic appearance of hypothalamic hypogonadism.