Huntington’s disease : hypothalamic, endocrine and metabolic aspects

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Huntington's disease (HD) is an autosomal dominant progressive, neurodegenerative disorder caused by an expanded trinucleotide (CAG) repeat sequence in the *HTT* gene. The nuclear symptoms and signs of HD consist of motor, cognitive and behavioural disturbances. Other less well-known, but prevalent and debilitating features of HD include unintended weight loss, sleep and circadian rhythm disturbances, as well as autonomic nervous system dysfunction. However, the pathogenesis of these less well-known features of HD is poorly understood and currently no effective treatment options are available. It is thus of paramount importance to elucidate the pathological basis of these symptoms and signs in order to design and apply more effective therapeutic interventions.

Recently, substantial dysfunction of the hypothalamus was reported in both human studies and various knock-in and transgenic animal models of HD. The hypothalamus consists of groups of interconnected neuronal nuclei located at the base of the brain that regulate a broad array of physiologic, homeostatic and behavioural activities. Therefore, in this thesis we attempt to substantiate the premise that hypothalamic dysfunction per se, as well as secondary (neuro)endocrine and metabolic alterations could contribute to the pathogenesis of several non-motor symptoms and signs of HD.

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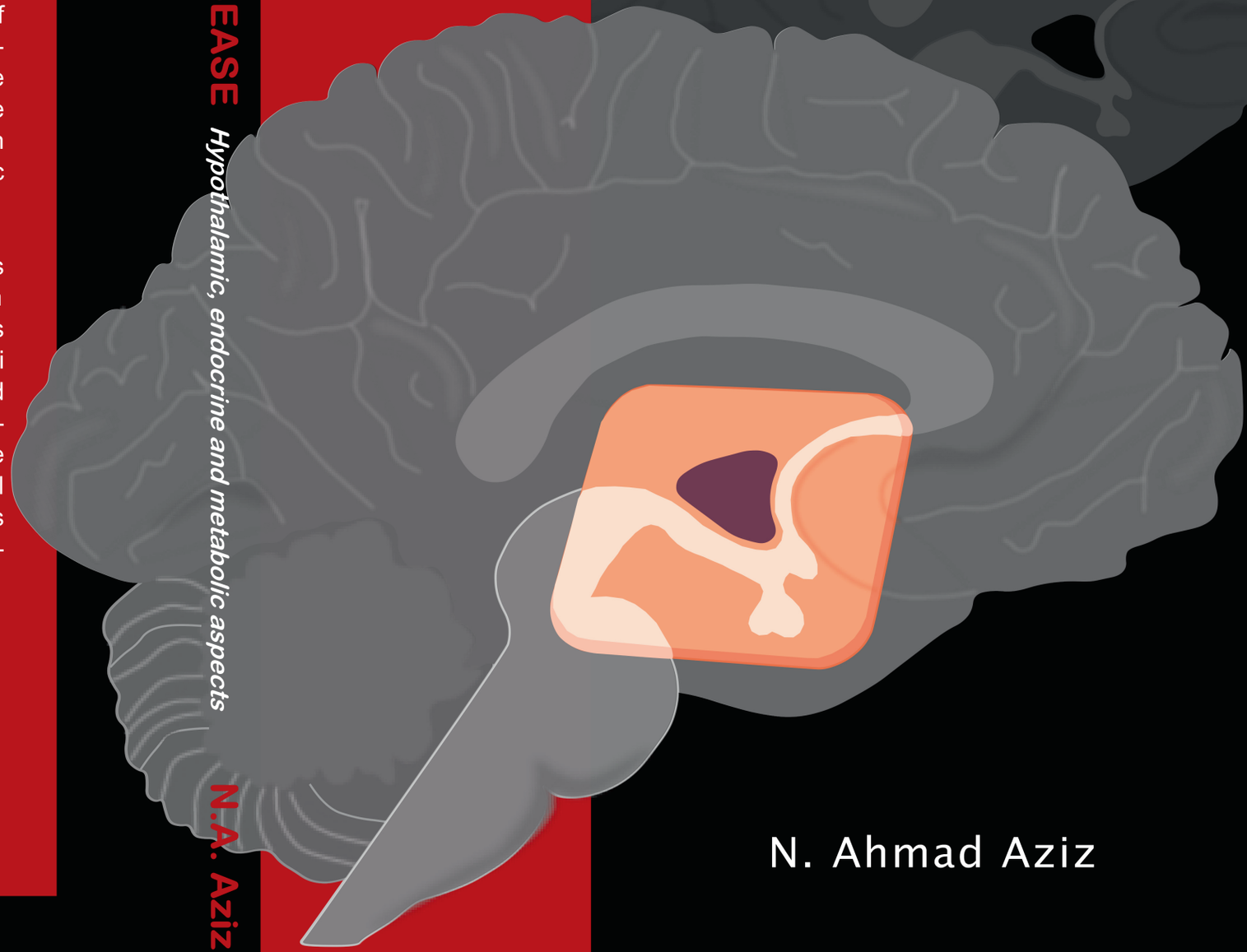

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