The differential diagnosis of the late-onset frontal lobe syndrome is challenging, especially when discriminating bvFTD from primary psychiatric disorders such as major depression, bipolar disorder and schizophrenia. Therefore, the Late Onset Frontal Lobe Syndrome study (LOF) was designed to develop a ‘new’ paradigm to tackle this clinical challenge. Patients were included between the age of 45-75 years with a frontal behavioural change consisting of apathy, disinhibition, or compulsive/stereotypical behaviour. In this current thesis, we investigate the prospective data of the LOF by using the two-year-follow-up final diagnosis as gold standard to investigate the baseline data for bvFTD and primary psychiatric disorders. In conclusion, we advocate the use of validated questionnaires for behavioural symptoms to assess stereotypical behaviour and to discriminate between symptoms of depression and apathy. Most of all, we emphasize the use of neuroimaging in patients with behavioural changes. In specific cases where the neuroimaging is not conclusive (no frontotemporal changes on MRI and \(^{18}\text{F}\) FDG-PET or only a positive \(^{18}\text{F}\) FDG-PET scan), we advocate genetic testing (C9orf72) and the use of CSF biomarkers (p-tau / tau ratio, NfL and YKL40) which can help to minimalize the diagnostic challenge. Overall, thoughtfulness is still highly recommended in these neuropsychiatric patients in combination with a multidisciplinary approach and an appropriate duration of follow-up.