

The term 'behavioural and psychological symptoms of dementia' (BPSD) describes a wide spectrum of disturbances accompanying the core cognitive deficit in dementia such as: psychosis, aggression, agitation, depression and/or anxiety. It is estimated that at least one or more symptoms of behavioural disturbances will manifest in almost all dementia patients in the course of their disease.

Currently, specifically targeted pharmacotherapies for BPSD are so far unavailable and current treatments are far from ideal since they involve the use of atypical antipsychotics, which have limited clinical effectiveness, cause serious side effects and are associated with increased risk of death in elderly patients. It should be highlighted that FDA approved atypical antipsychotics in the 1990s exclusively for the treatment of schizophrenia, thus young adult disease associated with distinct neurobiological deficits than BPSD.

In the view of lack of specifically targeted pharmacotherapies for BPSD, development of safe and effective treatment dedicated to the fragile population of elderly patients remains an unmet clinical need. It has been widely accepted that parallel modulation of multiple biological targets can be beneficial for the treatment of diseases with complex central nervous system (CNS) diseases. Indeed, a promising strategy to identify novel pharmacotherapeutics is the discovery of hybrid molecules that interact with 2 or more biological targets that are physiologically relevant to the disease. Considering these facts, the aim of this project is to obtain a library of hybrid molecules that combine activity at 5-HT<sub>6</sub> receptors and SERT, which may provide potentially beneficial treatment for BPSD.

In this project, we will synthesize a novel series of hybrid molecules that will be broadly characterized in a wide panel of in vitro assays and selected lead compounds will serve as pharmacological tools to verify the hypothesis that such receptor profile is suitable for the improved management of BPSD. The project presents original, interdisciplinary research focusing on the search for new compounds that display an interesting profile of activity. The project may significantly broaden the knowledge about the role of this molecular targets – aspects which are nowadays considered as highly promising in the future therapy of BPSD.