Summary

Using positron emission tomography (PET), it is possible to non-invasively image and quantify physiological/biochemical processes with picomolar sensitivity. A large range of processes can be studied depending on the PET tracer being used. Although PET allows for quantitative measurements of radioactivity concentrations, tracer kinetic models are required to “translate” these radioactivity measurements into quantitative assessments of physiological/biochemical processes.

In this thesis, the kinetic behaviour of novel biological tracers for activated microglia ^{18}F-DPA714) and NMDA receptors (^{11}C-GMOM and ^{18}F-PK-209) was investigated. The primary focus of the thesis was to quantify uptake of these molecular probes, which will be essential for longitudinal studies (progression of disease, response to therapeutic interventions). In many studies quantification of PET is performed using standardized uptake values (SUV) or, in the brain, SUV ratios (SUVr). Both SUV and SUVr are derived from a single (static) scan in which total uptake depends on several physiological processes, such as delivery (input function), blood flow, extraction, non-specific uptake and specific binding. Clearly, erroneous interpretation of SUV and SUVr is possible if one of these processes (other than specific binding) differs between subject groups or changes due to treatment. Knowledge of the kinetic behaviour of a tracer is essential to assess simplified methods, such as SUVr, that can be used in routine clinical practice. Hence, pharmacokinetic modelling is the first step when introducing a new tracer. When the optimal model is identified, this can subsequently be used to validate simplified approaches. Additionally, image processing techniques to improve the accuracy of PET studies are also presented, such as the development and validation of a new partial volume correction method in order to mitigate the quantitative biases due to the limited spatial resolution of PET images. In this thesis, all the steps were investigated for the novel radioligands mentioned above, that makes it possible to select the optimal method in terms of accuracy and simplicity for each specific clinical or research question.