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## Sigma-1 Receptor Imaging in the Brain

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## Stellingen

### *Behorende bij het proefschrift*

1. MicroPET studies of brain with  $^{11}\text{C}$ -SA4503 require kinetic modelling and metabolite analysis (Chapters 3, 6 and 7).
2. Aging affects sigma-1 receptors in the brain differently in different species and strains (Chapter 3)
3. When differences are not seen between groups due to huge variations in one group, it is possible that a separate subpopulation is included within it (Chapters 3 and 4).
4. Neither increase, nor decrease in sigma-1 receptor expression is good news (Chapters 4 and 5).
5. Dose dependent sigma-1 receptor occupancy by agonist drugs can be estimated using microPET and  $^{11}\text{C}$ -SA4503 (Chapters 6 and 7).
6. Combining pre-clinical PET studies with pharmacological studies and pharmacokinetic analysis can give valuable insights in to the relationship between tissue penetration, target engagement and pharmacological effect (Chapter 7).
7. Both extent and duration of receptor occupancy is important to the efficacy of sigma-1 agonist drugs (Chapters 7 and 8).
8. With biological processes often being non-linear, non-linear mixed effects modelling should be considered for PET data analysis (Chapter 9)
9. Sleep deprivation experiments are stressful to both the experimenter and the animals.
10. The drug industry needs to be educated about when to use imaging technology so that its involvement is built into the drug development program and not just as an afterthought to look at why things went wrong (Kevin Cox, CEO, Imanova).
11. Interim analysis can often save time, but it can also lead you on to tangents which take up even more time.
12. You don't need to see the flame to know the lamp is lit.
13. Running multiple projects at a time need not mean a faster PhD, especially when one of them is a baby.
14. If sleep deprivation or hormones are involved, there is most probably a role for sigma-1 receptors towards the cause of cognitive impairment in pregnancy and early parenthood (a.k.a "mummy brain").