Quantitative evaluation of peptide analogue distribution in mouse tissue using 3D computer modelling - DTU Orbit (11/08/2019)

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The use of automated image analysis of microscopy images is increasing to enable high throughput approaches and unbiased analysis of the increasingly large data sets produced. This thesis investigates the use of automated image analysis to quantify peptide analogue distribution in mouse brain tissue. The main group of peptides included in this work was glucagon-like peptide 1 receptors agonists (GLP-1RA) used for treatment in diabetes and obesity. Two main image modalities have been applied for image acquisition; Light Sheet Fluorescence Microscopy (LSFM), and slide scanner images of 2D histology sections. The work demonstrates the use of automated image analysis based on image registration to quantify LSFM data of the peptide brain distribution following peripheral administration. The methodology was expanded during the PhD work to also include study of receptor mapping and brain activation. The automated analysis was enabled by integration with a digital multimodality brain atlas from the Allen Institute of Brain Science (AIBS). The work showed that GLP-1RAs accessed multiple brain regions mainly in the hypothalamus and hindbrain and led to increased brain activation in regions related to decreased food intake. The developed integrated brain atlas provides a novel analysis approach for LSFM data to aid researchers understand the complex brain biology related to development of pharmaceuticals with brain mode of action.

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