Expression profiling in laser microdissected hippocampal subregions reveals large differences in expression between CA3 and DG subregions

Datson NA, Meijer L, Steenbergen P, Morsink M, De Kloet ER
Division of Medical Pharmacology, LACDR/LUMC, Leiden

We previously used both Serial Analysis of Gene Expression (SAGE) and DNA microarray technology to analyse gene expression in whole hippocampus (rat and mouse). However, only genes with an abundant to medium abundant expression throughout the hippocampus were detectable. Expression profiling in the hippocampus is hampered by it's cellular heterogeneity, resulting in expression of a large number of different genes and dilution of transcripts with a subregion-specific expression or regulation in the complex background of whole hippocampal tissue.
The aim of the present study was to evaluate the feasibility of using laser microdissected hippocampal subregions for expression profiling to improve detection of transcripts with a subregion-specific expression. CA3 and DG subregions were isolated in duplo from rat brain slices using laser microdissection, subjected to 2 rounds of linear amplification and hybridised to rat GeneChips containing approximately 8000 rat transcripts (RG_U34A; Affymetrix). Analysis of the data using SAM (Significance Analysis of Microarrays, Tusher et al., 2001) revealed 278 genes with a significant difference in expression between CA3 and DG with a false discovery rate of less than 1%, of which 88 had higher expression in DG and 190 higher expression in CA3. The fold-changes in expression ranged from 1.2 to 50-fold. Among the identified genes were several transcripts already known to display differential expression between the subregions, such as NT-3, GAP-43 and caldendrin, as well as numerous mRNAs and ESTs not yet known to show differential expression. A selection of these genes were validated by in situ hybridisation or Q-PCR. This data supports the idea that profiling in hippocampal subregions should improve detection of genes with a subregion-specific expression pattern or regulation.
Supported by NWO grant 903-42-085

Nicole Datson, Division of Medical Pharmacology, Leiden/Amsterdam Center for Drug Research, Leiden University, P.O. Box 9502, 2300 RA Leiden, The Netherlands, t 071-5276222, e-mail datson_n@lacdr.leidenuniv.nl

Neuroscience 1