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Topological comparison of receptor densities and mRNA expression in the cerebral cortex

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INTRODUCTION

In recent years, there were attempts to map the neuroreceptor distributions in the human brain to enlighten the molecular mechanisms underlying brain disorders [1]. Here, we investigate the potential of the use of the human transcriptome as a surrogate to proteomic data..

METHODS

We made use of autoradiography data, published by Zilles et al. [1], that was compared to three different transcriptomic data sets represented by microarray (mA) and RNA sequencing (RNA-seq) data sets, published by Allan Human Brain institute [2], and interpolated mRNA expression patterns (int-mA) [3]. Regional values for Brodmann areas (38 regions for int-mA, 37 regions for mA, and 16 regions for RNA-seq), extracted from transcriptomic data sets for each expression pattern (45 in total) associated with one of 15 receptors listed in Zilles et al. paper [1], were compared to receptor distributions using Spearman's rank correlation.

RESULTS

We found solid positive associations between autoradiography and microarray data sets e.g. serotonin 1A receptor (HTR1A), r=0.64 (Fig 1b) or GABA receptor subunit alpha-1 (GABRA1) r=0.59 as well as negative associations e.g. GABA receptor subunit alpha-3 (GABRA3) r=-0.62 (Fig 2a) or GABA receptor subunit alpha-5 (GABRA5) r=-0.57 (Fig 2b).
Besides, we discovered similar results by investigating the interpolated mRNA gene expression patterns for HTR1A r=0.64 (Fig 1b) or GABRA1 r=0.56. The same was a truth for the negatively associated targets GABRA3 r=-0.62 (Fig 2c) and GABRA5 r=-0.57.
Comparison to the RNA-seq data revealed a positive correlation for HTR1A r=0.72 (Fig 1c) and GABA B receptor 1 (GABBR1) (r=0.78). On the other hand, negative associations were found e.g. alpha-1A adrenoreceptor (ADRA1A) r=-0.69. However, most of the receptor distributions represented by autoradiography data showed weak or no relation with any of the transcriptomic data sets.

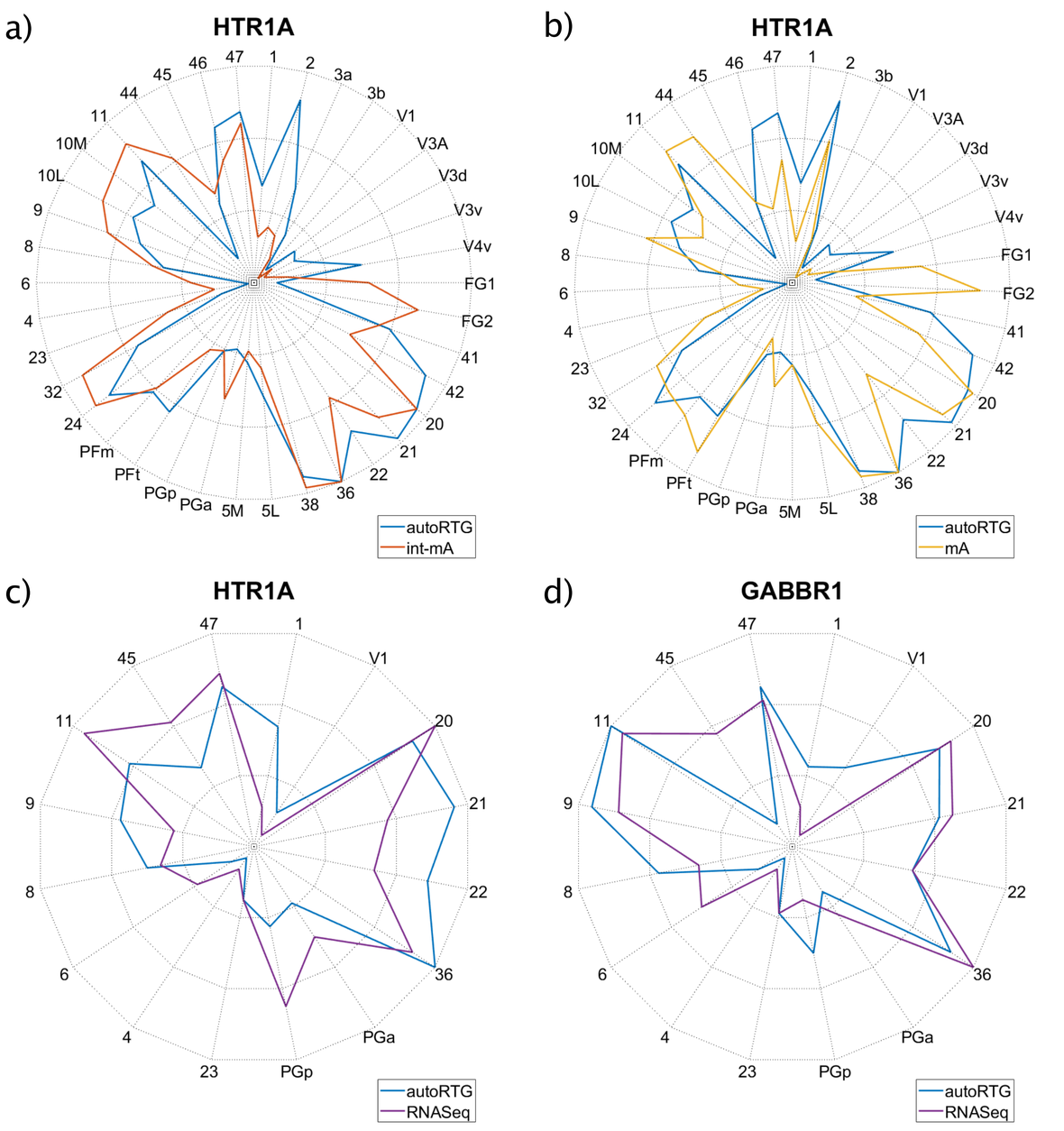

*Fig. 1: Radar plots showing the associations in different Brodmann areas for autoradiography data positively correlated with transcriptomic data for selected receptor distributions. Particularly, comparison of autoradiography data to **a)** interpolated mRNA expression for HTR1A, **b)** microarray data of HTR1A, **c)** RNA-seq data of HTR1A and **d)** RNA-seq data of GABBR1.*

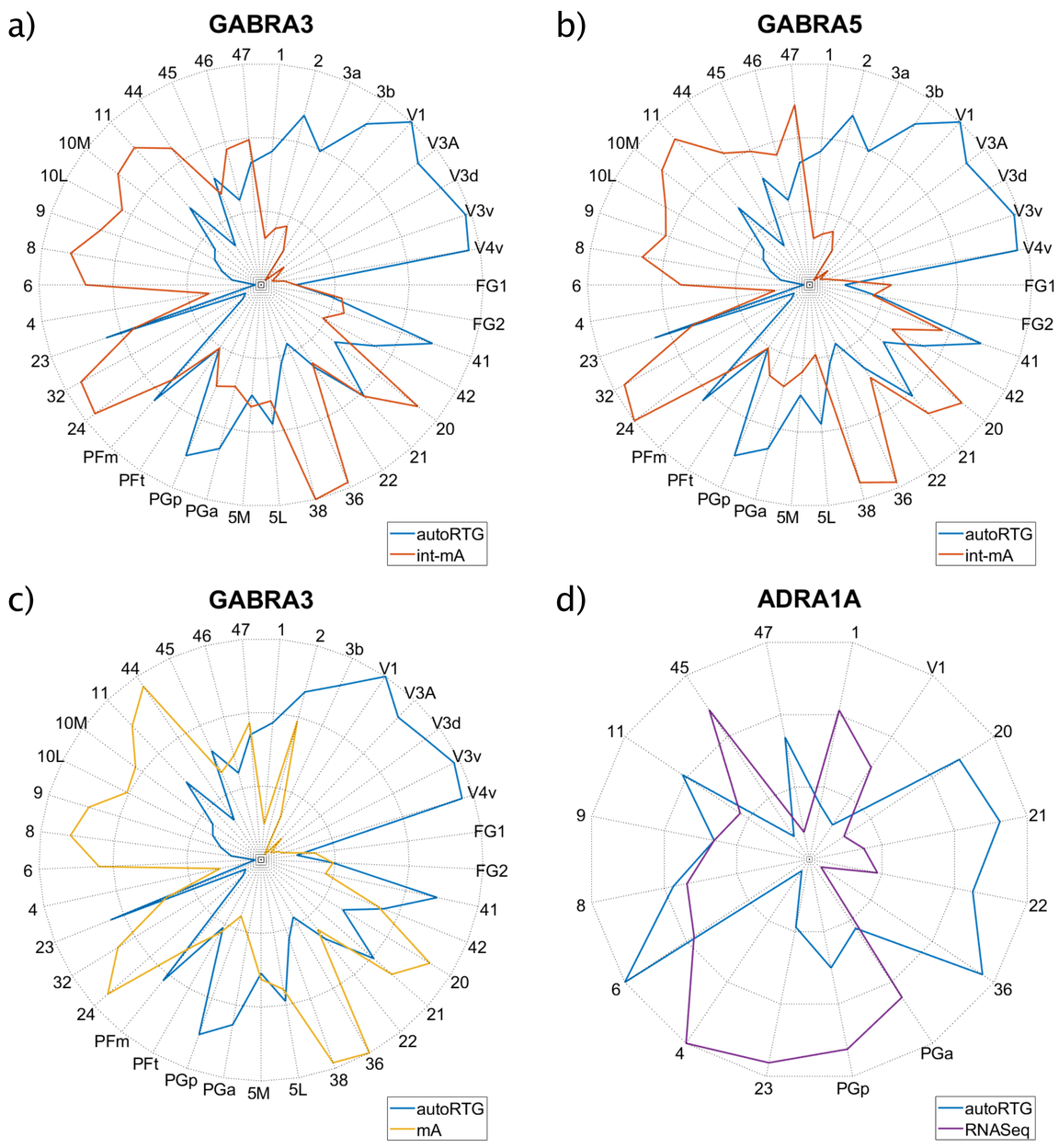

*Fig 2: Radar plots showing the associations in different Brodmann areas for autoradiography data negatively correlated with transcriptomic data for selected receptor distributions. Particularly, comparison of autoradiography data to **a)** interpolated mRNA expression for GARBA3, **b)** interpolated mRNA expression for GABRA5, **c)** microarray data of GABRA3 and **d)** RNA-seq data of ADRA1A.*

CONCLUSIONS

In this work, we were able to find a strong association between some of the receptor distributions and transcriptome. Nevertheless, as most of the receptor distributions were showing negative or no correlation with mRNA expression, our results highlight the importance of post-transcriptional processes and the investigation of potential mRNA markers indicating the strength of posttranscriptional transformations

ACKNOWLEDGMENT

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REFERENCES

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[2] Hawrylycz et.al. 2012, Nature 489: 391-399
[3] Gryglewski et al., 2018, NeuroImage 176: 259-267