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YAP and TAZ expression in benign pediatric brain tumors with high levels in choroid plexus papilloma

Laura Hero[1], Saskia Kuhl[1], Jill Dicke[1], Roland Goldbrunner[1], Marco Timmer[1]

1 Center for Neurosurgery, Department of General Neurosurgery, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne

Introduction

Yes-associated protein (YAP) and its paralogue Transcriptional co-activator with PDZ-binding motif (TAZ) are transcriptional co-activators affected primarily by mechanotransduction of the cell.[1] As effectors of the Hippo signaling pathway they control proliferation and apoptosis and by that regulate the physiologic sizes of organs and tissues.[2] An altered expression of YAP and TAZ could be linked to proliferation, invasion and metastasis of some malignancies, such as breast, gut, lung and liver cancer, thereby affecting the tumorigenesis and survival of patients.[1-4]

There is evidence that YAP and TAZ play a role in tumor development in the central nervous system.[2] In doing so, overexpression of YAP and TAZ is linked to poor differentiation in gliomas (WHO grade III and IV) and thus correlates with increased metastasis and lower survival rates of patients.[2,3,5]

Our goal was to examine how YAP and TAZ are expressed in different entities of benign pediatric brain tumors.

Methods

Tumor and control tissues were collected during neurosurgical resection and classified with WHO 2007 classification. YAP and TAZ expression was investigated via PCR and Western Blotting in a total of 24 samples from patients with pediatric low-grade tumors. Diagnoses included dysembryoplastic neuroepithelial tumor (DNET, n=3), choroid plexus papilloma (n=6), ganglioglioma (n=6), neurofibroma (n=4) and craniopharyngioma (n=5).

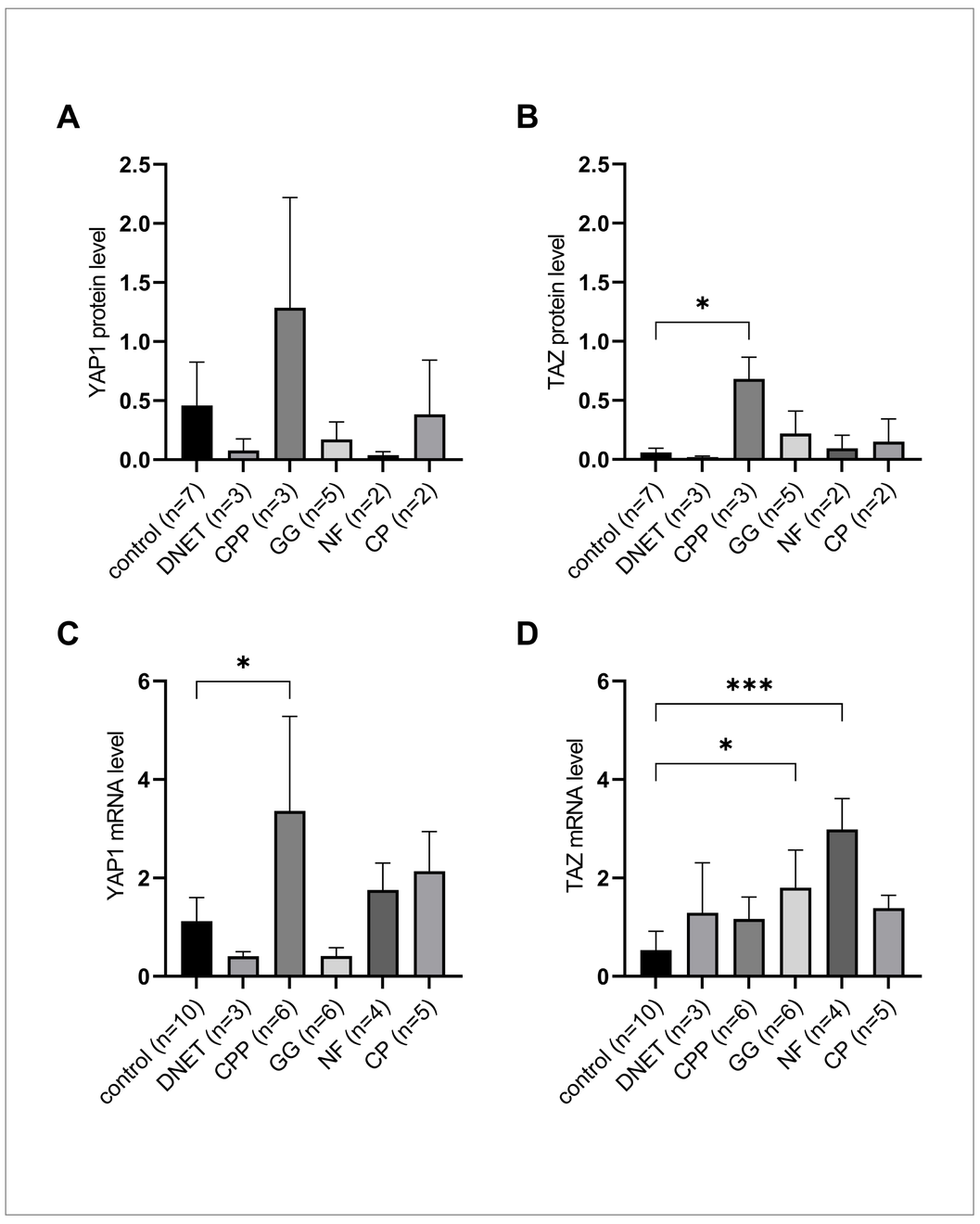

Fig. 1: Comparison of YAP and TAZ expression with control group

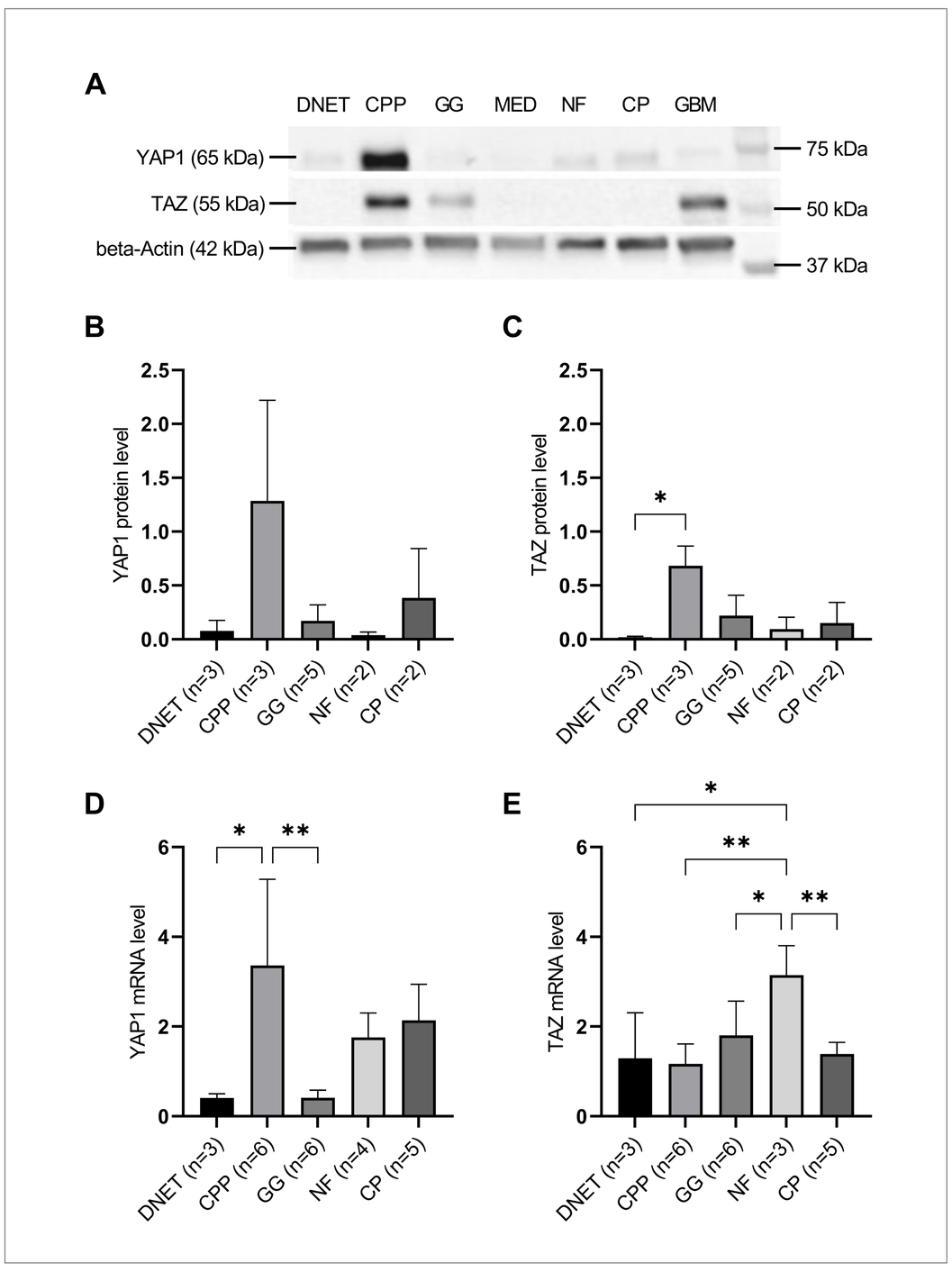

Fig. 2: Comparison of YAP and TAZ expression among tumor groups

Results

Expression of YAP and TAZ in different entities was first examined in comparison to the control group (Fig. 1). We then contrasted the expression ranks of each tumor with the other (Fig. 2).

Choroid plexus papilloma shows greater expression rates of YAP and TAZ

We found high protein expression of YAP and TAZ in choroid plexus papilloma. TAZ protein expression was significant compared to control tissue (z=2.582, adjusted p=0.0491, Kruskal Wallis test, Fig. 1A and 1B) and DNET (z=3.012, adjusted p=0.0259, Kruskal Wallis test, Fig. 2C). Western Blot bar marks of YAP and TAZ were also intensified in contrast to high-grade medulloblastoma and glioblastoma (Fig. 2A, quantitative data not shown). mRNA expression of YAP showed significant difference in choroid plexus papilloma compared to control tissue (z=2.969, adjusted p=0.0149, Kruskal Wallis test, Fig. 1C), DNET (z=3.100, adjusted p=0.0194, Kruskal Wallis test, Fig. 2D) and ganglioglioma (z=3.674, adjusted p=0.0024; Fig. 2D).

TAZ mRNA is expressed high in ganglioglioma and neurofibroma

Gangliogliomas and neurofibromas showed a significantly higher TAZ gene expression compared to the control group (z=3.3138, adjusted p=0.0085 and z=3.744, adjusted p=0.0009, Kruskal Wallis test, Fig. 1D). Neurofibroma group also showed significantly higher gene expression compared to every other group (DNET: q=5.107, adjusted p=0.0150; CPP: q=6.305, adjusted p=0.0025; GG: q=4.285, adjusted p=0.0494; CP: q=5.424, adjusted p=0.0093, One-way ANOVA; Fig. 2E).

Conclusion

Higher expression rates of YAP and TAZ could indicate a possible role of the Hippo pathway effectors in tumorigenesis of choroid plexus papilloma, ganglioglioma and neurofibroma. Conferring to our findings further investigation is necessary to determine, whether the transcription factors YAP and TAZ have an impact on cell proliferation, tumor progression or clinical outcome of patients with choroid plexus papilloma, ganglioglioma or neurofibroma.

References

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laura.hero@uk-koeln.de