Similar findings were reported by Corti et al., (2011). Upon post-mortem examination of the brains of 21 patients affected by schizophrenia and of 35 healthy controls, with an emphasis on mGluR5 expression in the PFC, no differences were found. Interestingly, it is the PFC which is primarily involved in executive functions such as decision making, working memory and learning which were observed to be hampered via disrupted mGluR5 signalling in animal models of schizophrenia, described earlier.

However, contrasting evidence comes from studies involving schizo-affective patients. Schizoaffective disorder is mainly characterised by positive psychotic symptoms, disordered thought processes and abnormal fluctuations in mood, distinguishing it from schizophrenia (Malaspina et al., 2013).

Volk et al., (2010) looked at post-mortem PFC brain tissue from a sample of 28 schizophrenic patients, 14 schizoaffective patients and 42 healthy controls. While mGluR5 expression was not altered in schizophrenics compared to controls, there was reduced mGluR5 expression in schizoaffective patients. It may be tentatively hypothesised from this, that reduced expression is reduced in schizoaffective patients due to its role in the more mood-related symptoms of schizophrenia such as asociality.

While mGluR5 expression is unaltered in schizophrenia, Ohnuma et al., (1998) discovered reduced glutamate transporter expression, thereby indicating decreased glutamate neurotransmission and less functional glutamate. The findings from these post-mortem studies indicate that the role of mGluR5 in schizophrenia in humans is not structural. Instead, they appear to favour the idea of mGluR5 functional anomalies in the symptoms of schizophrenia.
Conclusions & Future directions

Therefore, it may be surmised that mGlur5 may prove to be a target for future developments in the pharmacotherapy, through the use of mGlur5 PAMs, due to its role in the potentiation of NMDA, as the evidence discussed in this essay emphasises.

Also, in spite of their positive therapeutic effects, mGlur5 PAMs have had negative effects in rats receiving oral doses of 5PAM523 (4-Fluorophenyl){(2R,5S)-5-[5-(5-fluoropyridin-2-yl)-1,2,4-oxadiazol-3-yl]-2-methylpiperidin-1-yl}methanone) such as convulsions, neuronal cell death and abnormal mouth-movements (Parmentier-Batteur et al., 2013). Such issues need to be resolved before human testing can be conducted (Cioffi, 2013). Thus, while research findings are promising, mGlur5 PAMs have yet to reach clinical trial stage in human subjects.

In conclusion, there is significant evidence in favour of mGlur5-based treatments for schizophrenia, but until this evidence from animal studies is substantiated by similar evidence from human studies, novel therapeutics utilising mGlur5 PAMs need to be approached with some degree of caution.


