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Serotonin 2A receptor and its association with the pathology of schizophrenia

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Abstract

Dear Editor: Accumulated evidence suggests that serotonin 2A (5-HT2A) receptors are implicated in the pathology of schizophrenia. However the results remain inconclusive, particularly in the case of binding studies using postmortemtissue.We agreewith Dean's comment that our recent paper (Kang et al., 2009) reported a decrease in the density of [3H] ketanserin binding to the 5-HT2A receptors in the superior temporal gyrus (STG), which supported earlier findings in the planum temporal cortex (Pralong et al., 2000), despite Burnet et al. reporting previously that there was no change in [3H] ketanserin binding in the STG in schizophrenia (Burnet et al., 1996).....

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SEROTONIN 2A RECEPTOR AND ITS ASSOCIATION WITH THE PATHALOGY OF SCHIZOPHRENIA

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Dear Editor:

Accumulated evidence suggests that serotonin 2A (5-HT_{2A}) receptors are implicated in the pathology of schizophrenia. However the results remain inconclusive, particularly in the case of binding studies using postmortem tissue. We agree with Dean's comment that our recent paper (Kang et al., 2009) reported a decrease in the density of [^{3}H] ketanserin binding to the 5-HT_{2A} receptors in the superior temporal gyrus (STG), which supported earlier findings in the planum temporal cortex (Pralong et al., 2000), despite Burnet et al. reported previously that there was no change in [^{3}H] ketanserin binding in the STG in schizophrenia (Burnet et al., 1996). The controversy has also been the case in studies on [^{3}H] ketanserin binding density in the dorsolateral prefrontal cortex and hippocampus in schizophrenia, even when reports have arisen from the same laboratory (Scarr et al., 2004, Matsumoto et al., 2005) and using tissue from same cohort of subjects (Dean and Hayes, 1996, Dean et al., 1996). Recently, Dean and his colleagues have provided evidence to show that confounding [^{3}H] ketanserin binding results in the dorsolateral prefrontal cortex of schizophrenia subjects were due to the employment of different methodologies, whereby a decrease in [^{3}H] ketanserin binding in the dorsolateral prefrontal cortex in schizophrenia could only be detected by binding experiments on tissue sections and in crude homogenate, not on washed membranes (Dean et al., 2008). Dean and colleagues tried to extend this finding to the whole CNS (Dean et al., 2008), however this extension was not supported by their results in the STG and hippocampus (Pralong et al., 2000, Scarr et al., 2004, Matsumoto et al., 2005). Using tissue from the same cohort of subjects for studies in the dorsolateral prefrontal cortex, Dean and colleagues observed a decrease in the density of 5-HT_{2A} receptors in the STG of

schizophrenia subjects using [^{3}H] ketanserin binding techniques in both tissue sections and washed membranes (Pralong et al., 2000); findings that were opposite to those reported in the dorsolateral prefrontal cortex (Dean and Hayes, 1996, Dean et al., 1996). Even more interesting, the B_{max} measured by both binding methods used in the STG were significantly correlated (r^2 = 0.501, p=0.024) (Pralong et al., 2000). On the other hand, decreased [^{3}H] ketanserin binding in the hippocampus was reported in one of their studies (Scarr et al., 2004) but not the other (Matsumoto et al., 2005), despite using the same binding method (ie: in tissue sections). Unfortunately, these opposing results appear to be omitted in Dean's comments and earlier paper (Dean et al., 2008). Therefore, if these results are correct, caution should be given if extending the findings reported in the dorsolateral prefrontal cortex to other CNS regions.

As various neurotransmitter receptor systems (eg. dopamine D2, $GABA_A$, 5-HT_{2A} etc. receptors) are involved in the pathology of schizophrenia (Wong and Van Tol, 2003), it is important to understand how these neurotransmitter systems interacted. We recognized that Dean has made a contribution in revealing the relationships among dopamine D2, $GABA_A$, 5-HT_{2A}, and muscarinic M1 receptor alterations in the dorsolateral prefrontal cortex in schizophrenia (Dean, 2001). Our recent studies of the pathological changes of $GABA_A$, 5-HT_{2A}, and muscarinic M1 receptors in the STG (Deng and Huang, 2005, Deng and Huang, 2006, Deng et al., 2007, Kang et al., 2009) provide an opportunity for us to explore the relationships among these receptors in the STG and their possible roles in the pathology of schizophrenia. Regarding the present study, we would like to clarify that, schizophrenia and control data were combined due to the relative low sample size (8

schizophrenia subjects and 8 controls), and Spearmans correlation test was employed to assess the relationships between the bindings of various receptors (Kang et al., 2009). We would also take this opportunity to correct a typographical error in the correlation between 5-HT_{2A} and $GABA_A$ receptors (corrected to r=-0.47, p=0.066). These correlation data represent possible interactions between these receptors, and we agree with Dean's comments that one should be cautious when interpreting these relationship results. Further studies to identify the mechanisms for the interactions between various neurotransmitter receptors would largely contribute to revealing the pathology of schizophrenia.

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