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Effects of treatment of schizophrenia on microglia: a [11C]PK11195 PET study

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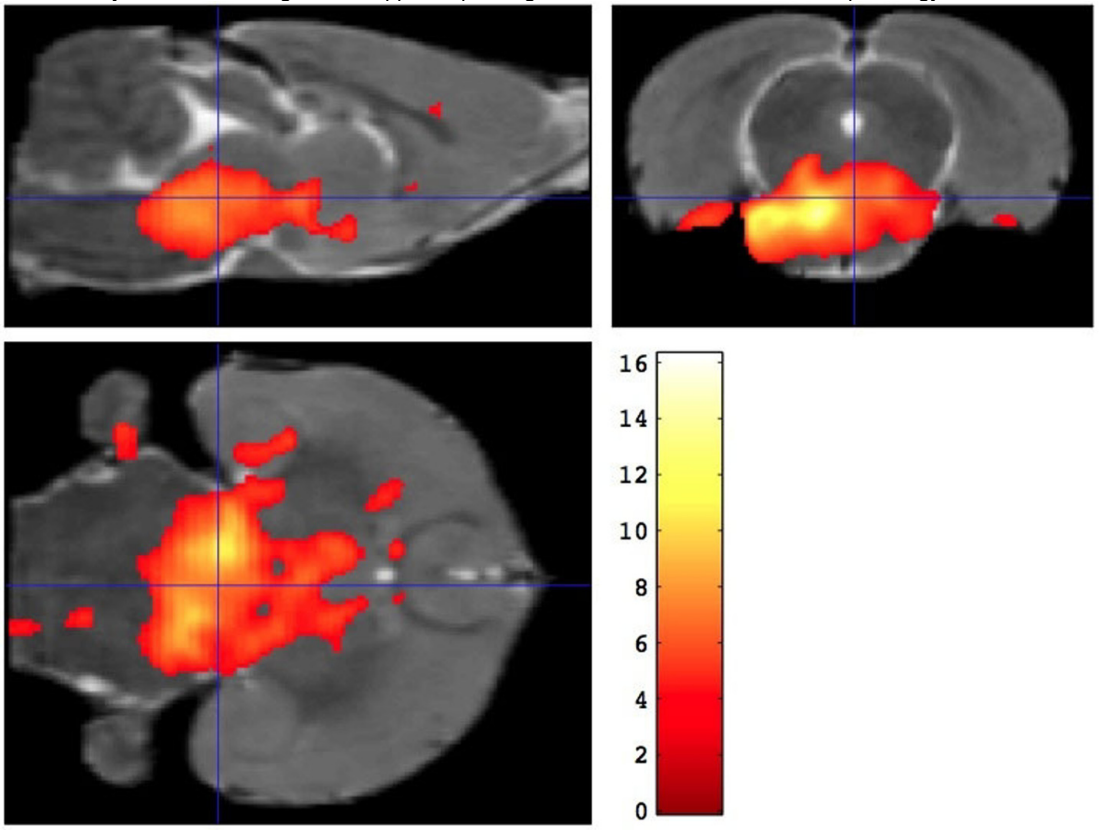
Microglia express the TSPO (TranSlocalor PrOtein) receptor formerly known as the PBR (peripheral benzodiazepine receptor). The densitiy of the TSPO is dependent on the inflammatory state of microglia. The radiopharmaceutical [^{11}C]PK11195 binds in excess to the TSPO in activated microglia. We showed that the hippocampus of psychotic patients experienced significantly more [^{11}C]PK11195 binding than the hippocampus of healthy controls. To elucidate the effect of antipsychotic medication on brain inflammation the herpes encephalitis rat model was chosen, because of pathophysiological similarity: Herpes simplex virus preferentially infects hippocampus. In adult rats 10E5 pfu of HSV-1 (clinical strain) was administered intranasally. After 3-5 days sickness behavior developed. At the 6th day and at the 13th day after inoculation a [^{11}C]PK11195 PET scan was performed. Drugs were delivered by osmotic minipumps(haloperidol, clozapine, saline). Only clozapine treatment delayed sickness behavior. Clozapine treatment reduced the inflammation in the mesecephalon and immediate surrounding regions after 6 days and reduced dissemination of inflammation to brain cortex at 13 days after inoculation. Conclusion: In a herpes infection model clozapine exerts potent anti-inflammatory effects on microglia. The hippocampus might be the link between infectious pathology and inflammation in schizophrenia patients.



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