

Gene*environment interactions in the development of prepulse inhibition.

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Schizophrenia is a severe psychiatric disorder afflicting approximately 1% of the general population. Patients suffer among others from information processing deficits such as reductions in prepulse inhibition and acoustic (P_{50}) sensory gating. Since such processes can also be investigated in rats or mice, they have often been used to investigate aspects of schizophrenia in animals. There now appears to be general agreement that the so-called 'three-hit hypothesis' can best explain the etiology of schizophrenia. According to this theory genetic factors (I) interact with pre and/or early postnatal factors (II) to increase the liability for developing psychotic symptoms. Late life environmental factors (III) are needed to change this liability into a full-fledged psychiatric disorder. However, the exact nature of each of these different factors is still largely unknown and will be difficult to study in humans. In animals, on the other hand, such factors can easily be applied in a controlled design. Using prepulse inhibition and acoustic sensory gating measures we can investigate to what extent genetic, early and late environmental factors can induce abnormalities also seen in schizophrenic patients.

So far most studies have focussed on the genetic and early environmental factors, and studies have shown that specific genetic alterations (such as the dopamine transporter knockout) or early stress (such as a 24 hr period of maternal deprivation) can lead to a significant reduction in prepulse inhibition. So far very few studies have investigated the effects of late life environmental factors, but some data from other studies have shown that pubertal cannabinoid treatment or stress just before testing can reduce prepulse inhibition under certain conditions. This shows that indeed all three factors independently affect prepulse inhibition. The first studies that investigate the interaction between these three factors are now being published and will be discussed.

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