2011 ECETOC YOUNG SCIENTISTS AWARD

Supported by ECETOC for toxicological research into mechanisms and risk assessment

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P2317

DIFFERENTIAL EFFECTS OF METHYLAZOXYMETHANOL AND MK-801 ADMINISTRATION ON LEARNING AND MEMORY IMPAIRMENT IN SPRAGUE DAWLEY AND WISTAR HAN RATS

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Wistar Han (WH) and Sprague Dawley (SD) rats are the preferred strains for Europe and the US, respectively, though both are acceptable for EU and US test guidelines. Potential differences in behavioral performance between the strains have not been extensively investigated, though unexpected differences between strains could complicate risk assessment. Learning and memory testing was conducted within a developmental neurotoxicity study. Three groups were used for each strain. F0-females received saline or 20 mg/kg Methylazoxymethanol (MAM; known to produce neuropathic and behavioral alterations in offspring) intra-peritoneally on gestation Day15. Animals littered, and offspring were tested in the Biel maze at weaning (PNDs 22-28) or adulthood (PNDs 62-68). On days of testing, animals were given saline or 0.1mg/kg MK-801, which impairs learning and memory performance. Animals swam 'path A,' were then switched to an alternative 'path B,' and were last switched back to 'path A' for the memory test. Time to escape the maze and number of errors were quantified. Both strains learned each path, both remembered 'path A' when tested, and both were impaired with MK-801 administration. However, strain differences were evident: in general, SD rats learned better than WHs (taking less time and making fewer errors). They were also more impaired with MAM treatment, with more time and errors than WHs. Conversely, WH rats were more impaired with MK-801 administration, especially over 'path B'. In conclusion, these data highlight differences in general test performance and in drug sensitivity between the strains, which could ultimately require consideration in risk assessment.