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Final Technical Report

Michael Davis

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Publications:

Davis, M. Apomorphine, d-amphetamine, strychnine and yohimbine do not alter prepulse inhibition of the acoustic startle reflex. Psychopharmacology, 1988, 95, 151-156.

Rosen, J.B. and Davis, M. Temporal characteristics of enhancement of startle by stimulation of the amygdala. Physiology and Behavior, 1988, 44, 117-123.

Yeomans, J.S., Rosen, J.B., Barbeau, J. and Davis, M. Double-pulse stimulation of startle-like responses in rats: Refractory periods and temporal summation. Brain Research, 1989, 486, 147-158.

Davis, M. Sensitization of the startle reflex by footshock. Behavioral Neuroscience, 1989, 103, 495-503.

Boulis, N.M. and Davis, M. Sensitization by footshock of startle responses elicited electrically from different points along the acoustic startle pathway. Behavioral Neuroscience, 1989, 103, 504-508.

Hitchcock, J.M., Sananes, C.B. and Davis, M. Sensitization of the startle reflex by footshock: Blockade by lesions of the central nucleus of the amygdala or its efferent pathway to the brainstem. Behavioral Neuroscience, 1989, 103, 509-518.

Davis, M., Commissaris, R.L., Wagner, K.R., Yang, S., Kehne, J.H., Cassella, J.V., and Boulis, N.M. Spinal vs. supraspinal sites of action of the α_2 agonists clonidine and ST-91 on the acoustic startle reflex. Pharmacology, Biochemistry & Behavior, 1989, 33, 233-240.

Davis, M., Schlesinger, L.S., and Sorenson, C.A. Temporal specificity of fear conditioning: Effects of different CS-US intervals on the fear-potentiated startle effect. Journal of Experimental Psychology: Animal Behavioral Processes, 1989, 15, 295-310.

Campeau, S. and Davis, M. Reversible neural inactivation by cryogenic blockade in anesthetized and freely behaving rats. Journal of Neuroscience Methods, 1990, 32, 25-35.

Miserendino, M.J. D., Sananes, C.A., Melia, K.R., and Davis, M. NMDA antagonists in the amygdala block acquisition but not expression of conditioned fear-potentiated startle. Nature, 1990, 345, 716-718.

Davis, M., Mansbach, R.S., Swerdlow, N.R., Campeau, S., Braff, D.L., and Geyer, M. Apomorphine disrupts the inhibition of acoustic startle induced by weak prepulses in rats. Psychopharmacology, 1990, 102, 1-4.

Boulis, N.M. and Davis, M. Blockade of the spinal excitatory effect of cAMP on the startle reflex by intrathecal administration of the isoquinoline sulfonamide H-8: Comparison to the C-kinase inhibitor H-7. Brain Research, 1990, 525, 198-204.

Boulis, N.M., Kehne, J.H., Miserendino, M.J.D. and Davis, M. Differential blockade of early and later components of acoustic startle following intrathecal infusion of 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX) or DL-2-amino-5-phosphonovaleric acid (AP5). Brain Research, 1990, 520, 240-246.

Rosen, J.B. and Davis, M. Enhancement of electrically elicited startle by amygdaloid stimulation. Physiology and Behavior, 1990, 48, 343-349.

Campeau, S., Liang, K.C., and Davis, M. Long-term retention of fear-potentiated startle following a short training session. Animal Learning and Behavior, 1990, 18, 462-468.

Davis, M. The role of the amygdala and its efferent projections in fear and anxiety. In: Psychopharmacology of Anxiety, Oxford University Press, Oxford, 1989, pp. 52-79.

Davis, M. Neural systems involved in fear-potentiated startle. In "Modulation of Defined Vertebrate Neural Circuits, M. Davis, B.L. Jacobs, R.I. Schoenfeld (Eds), Annals of the New York Academy of Sciences, 563, 1989 pp 165-183

Davis, M. Pharmacological and anatomical analysis of fear conditioning. In: "Neurobiology of Drug Abuse: Learning and Memory". National Institute on Drug Abuse Research Monograph 97, 1990, pp. 126-165.

Davis, M. Animal models of anxiety based on classical conditioning: The conditioned emotional response (CER) and the fear-potentiated startle effect. Pharmacology and Therapeutics, 1990, 47, 147-165.