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The results of this study show a remarkable similarity between the treatment with acetyl-L-carnitine and a slope factor of 1.65. For the high slope factors found, we hypothesize that:

1) an interaction of thiopental with the receptor complex in rat brain homogenates [2]. The sigmoid E₅₀ model was fitted to both datasets. In vivo thiopental suppressed the withdrawal responses with an IC₅₀ of 28 μM and a slope factor of 1.65. The results of this study show a remarkable similarity between the in vivo curves and the in vitro curves, concerning both the effective concentrations and the shape of the curves. Based on this similarity we hypothesize that:

1) an interaction of thiopental with the GABA_A receptor complex can account for the inhibition of the withdrawal response; this relationship is linear. 2) two thiopental molecules bind to the GABA_A receptor complex with a positive cooperative effect on the (negative) modulation of the [³H]TBOB binding site. This can account for the high slope factors found.


The aim of this study was to gain insight into the molecular mechanism underlying the in vivo effects of thiopental. We compared the dose-response curve of thiopental on the withdrawal reflex to transcutaneous stimulation in rats [1] to the dose-response curve of thiopental on the binding of [³H]TBOB to the GABA_A receptor complex in rat brain homogenates [2]. The sigmoid E₅₀ model was fitted to both datasets. In vivo thiopental suppressed the withdrawal responses with an ED₅₀ of 4.5 mg/kg corresponding to 9.2 μmoles/kg brain, and a slope factor of 1.60. In vitro thiopental inhibited [³H]TBOB binding with an IC₅₀ of 28 μM and a slope factor of 1.65. The results of this study show a remarkable similarity between the in vivo curves and the in vitro curves, concerning both the effective concentrations and the shape of the curves. Based on this similarity we hypothesize that:

1) an interaction of thiopental with the GABA_A receptor complex can account for the inhibition of the withdrawal response; this relationship is linear. 2) two thiopental molecules bind to the GABA_A receptor complex with a positive cooperative effect on the (negative) modulation of the [³H]TBOB binding site. This can account for the high slope factors found.


IN VIVO EFFECTS OF THIOPENTAL.
A COMPARISON BETWEEN IN VITRO AND IN VIVO EFFECTS OF THIOPENTAL.
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The results of this study show a remarkable similarity between the in vivo curves and the in vitro curves, concerning both the effective concentrations and the shape of the curves. Based on this similarity we hypothesize that:

1) an interaction of thiopental with the GABA_A receptor complex can account for the inhibition of the withdrawal response; this relationship is linear. 2) two thiopental molecules bind to the GABA_A receptor complex with a positive cooperative effect on the (negative) modulation of the [³H]TBOB binding site. This can account for the high slope factors found.


EFFECTS OF CHRONIC DIAZEPAM ON EEG AND MOTOR BEHAVIOR OF THE RAT
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We evaluated the effect of chronic diazepam during 21 days on motor behavior and on the spectral content of the EEG of the WAG/Rij rat. The animals subcutaneously received silastic tubes either empty or filled with diazepam (50 mg/kg/day) resulting in constant blood concentrations (± 200 ng/ml). EEG's were filtered between 1-100 Hz and sampled with a frequency of 200 Hz. Two baselines were determined using an accelerod. The muscle tone was blindly scored on a two point scale via direct palpation. Post-drug recording was taken 9 days after tube removal. The spectral content was determined by FFT for 10 periods of 3.2 s of EEG accompanying passive wakefulness. Motor coordination was determined using an accelerometer. The muscle tone was blindly scored on a two point scale via direct palpation. Diazepam induced an increase in the power of the higher frequencies of the EEG (12-50 Hz) and a decrease in the power of the lower frequencies (1-8 Hz). No tolerance developed to this effect of diazepam. Diazepam induced a decrease in the accelerated performance. Tolerance to this effect was found on the 3rd day. The drug induced a decrease in muscle tone. No tolerance to this effect was found.

We conclude from these observations that functional tolerance is present. Our data exclude as a cause global decremental processes. We therefore hypothesize that the animal invokes oppositional processes in order to compensate for those effects of diazepam which impair its normal functioning.