ACUTE EFFECTS OF 1-METHYL-4-PHENYL-1,2,3,6-TETRAHYDROPYRIDINE (MPTP) ON BODY TEMPERATURE OF VARIOUS STRAINS OF MICE

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INTRODUCTION

Systemic administration of the neurotoxin MPTP to experimental animals induces the selective destruction of the nigrostriatal dopamine (DA) system. This MPTP-induced toxicity requires conversion of MPTP to its active metabolite, 1-methyl-4-phenylpyridine (MPP+), by the mitochondrial enzyme monoamine oxidase B-form (MAO-B). This selective MPTP neurotoxicity is accounted for by active MPP+ accumulation into DA neurons via the high affinity DA uptake system. The mitochondria, in addition to being the site for MPP+ formation, may also be an important target of MPP+ neurotoxicity, since MPP+ inhibits mitochondrial respiration, resulting in prevention of ATP formation with consequent cell death in the DA system. The MPTP-treated primates represent the best model currently available for study of the etiology of Parkinson's disease.

We earlier reported findings that a single systemic or direct injection of MPTP or MPP+ into albino mouse (ddY) brain markedly changed the body temperature, and we viewed this as an acute pharmacological effect. For example, a single systemic MPTP administration caused marked hyperthermia, mediated by peripheral cholinergic functions, followed by subsequent long-lasting, centrally mediated hypothermia. As noted earlier and above, for MPTP neurotoxicity, primates are more sensitive than rodents; and, in addition, the sensitivity to MPTP varies from species to species as well as between different strains of mice. Even in animals with low sensitivity, MPTP treatment results in differences in striatal content of DA and its metabolites, in DA accumulation by striatal synaptosomes, and in cell loss, depending on the strains of mice used, doses, duration of treatment, and dosing intervals. The present study was undertaken to clarify whether various strains of mice also show different sensitivity to a single MPTP injection in terms of the thermal effects.

MATERIALS AND METHODS

In this study, six different strains of male mice, ddY, BALB, ICR, C57BL, B6C3F1, and C3H, weighing 25±2 g, were used. Changes in rectal
temperature were recorded as described previously. Each group of ten mice with rectal temperature between 37.0-38.0 °C were selected and then maintained 1 hr to acclimatize them to ambient environment in a temperature-controlled room before injection of drug(s). Contents of DA, 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), 5-hydroxytryptamine (5-HT), and 5-hydroxyindoleacetic acid (5-HIAA) in mouse hypothalamus were determined by HPLC with ECD. MPTP was injected at a fixed dose of 24 mg/kg (i.p.).

RESULTS

Fig. 1 shows the time courses of changes in rectal temperature caused by a single MPTP injection (24 mg/kg, i.p.) into six different albino and pigmented mouse strains. The temperature was recorded at various times over a 7-hr period. This MPTP dose remarkably changed rectal temperature in two phases; in the first an increase occurred and in the second, a decrease. In general, the MPTP-induced hyperthermic effect was more marked in albino ddY, BALB, and ICR mice, but the subsequent hypothermia was more marked in the pigmented C57BL, B6C3F1, and C3H mice. Pretreatment of these six strains of mice with

![Graph showing changes in rectal temperature over time](image)

Fig. 1. Effects of i.p. administration of MPTP (24 mg/kg) on mouse rectal temperature in the six different strains. Rectal temperature was determined after MPTP administration at the various times indicated. ○: Saline (n=10), ●: MPTP24mg/kg (n=10). *:p<0.05, **:p<0.01 significant difference from saline-treated control.