Quebec Cooperative Study
of Friedreich's Ataxia

Glutamate and Aspartate Do Not Modify the Ataxic Gait of Acrylamide Treated Animals

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SUMMARY: *The purpose of this experiment was to examine the effects of intraventricular injections of glutamate and aspartate on the gait of animals rendered ataxic by the administration of acrylamide. Contrary to their previously reported corrective influence on ataxia induced by 3-acetyl pyridine, these amino acids did not modify the ataxic gait of acrylamide treated animals. This suggests that glutamate and aspartate can act in cerebellar but not in peripheral types of ataxia in animals.*

RÉSUMÉ: *Le but des expériences présentes est d'examiner l'effet d'injections intraventriculaires de glutamate et d'aspartate sur la démarche d'animaux rendus ataxiques par l'administration d'acrylamide. Les acides aminés employés n'exercèrent pas leur influence correctrice sur l'ataxie causée par l'acrylamide, contrairement à ce qui s'était passé dans l'ataxie par 3-acetyl-pyridine. Ces résultats suggèrent que le glutamate et l'aspartate peuvent agir chez les animaux ataxiques de type cérébelleux, mais non de type périphérique.*

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INTRODUCTION

In a previous report we demonstrated that intraventricular injections of glutamate and aspartate can reverse the abnormal gait of rats rendered ataxic by the administration of 3-acetyl-pyridine (3-AP) (De Michele et al, 1980). Since the prominent neuropathological change caused by 3-AP is the destruction of the inferior olivary nucleus and of the climbing fibers to the cerebellum, this treatment constitutes a model of cerebellar ataxia (Desclin and Escubi 1974). Therefore, it seemed warranted to determine if the observed effects of glutamate and aspartate are specific to this type of ataxia or if these amino acids could also correct the ataxia induced by a neurotoxin having a different mechanism of action.

Administration of acrylamide to animals results mainly in a peripheral neuropathy characterized by hindlimb paralysis, foot drop and an ataxic gait (Kuperman 1958, Jolicoeur et al, 1980). Histopathological changes produced by acrylamide consist of distal axonal degeneration of peripheral motor and sensory nerve cells (Spencer and Schaumberg 1974, Gipon et al, 1977). The purpose of the present experiment was to examine the effects of glutamate and aspartate on the ataxic gait of acrylamide treated animals.

METHODS

Thirty male albino rats, 250-300 g in weight, were used. They were implanted, under pentobarbital anesthesia, with an indwelling cannula (26 gauge) into the left brain ventricle. A recovery period of at least 48 hours was given before treatments were initiated. Animals were injected intraperitoneally with 50 mg/kg acrylamide daily for four days. Acrylamide (J.T. Baker Chemical Co.) was dissolved with 0.9 percent NaCl to obtain an injection volume of 1 ml/kg. Twenty-four hours after the last acrylamide injection, the animals' walking patterns were measured by calculating the angle between consecutive and contralateral steps according to a procedure previously described (Jolicoeur et al, 1979). After a first recording of gait patterns, animals were injected intraventricularly with either 0.9 percent NaCl, 1.32 μM glutamate, or μ1.32 M aspartate. Animals' gaits were then measured immediately following injections and 1 hour after. Glutamate and aspartate were dissolved in 0.9 percent NaCl and Ph of solutions was adjusted with sodium hydroxide. Intraventricular injections were performed by means of a 50 μl Hamilton syringe, linked to the animals cannula with PE-20 polyethylene tubing. Volumes of injections were 10 μl, given over a 30 sec. period.

RESULTS

Data were analysed by a two way ANOVA for repeated measures (Winer 1971). Factors included in the analysis were injections and test periods. Each of the three intraventricular injections given, 0.9 percent NaCl, glutamate and aspartate, constituted one level of the injection factor. Each of the gait measurements performed before, immediately after and 1 hour after injections, contributed to one level of the test period factor. Main effects for injections and test periods were not significant ($P > 0.05$). The interaction injections by test period was also not significant ($P > 0.05$). Results of this experiment are summarized in figure 1

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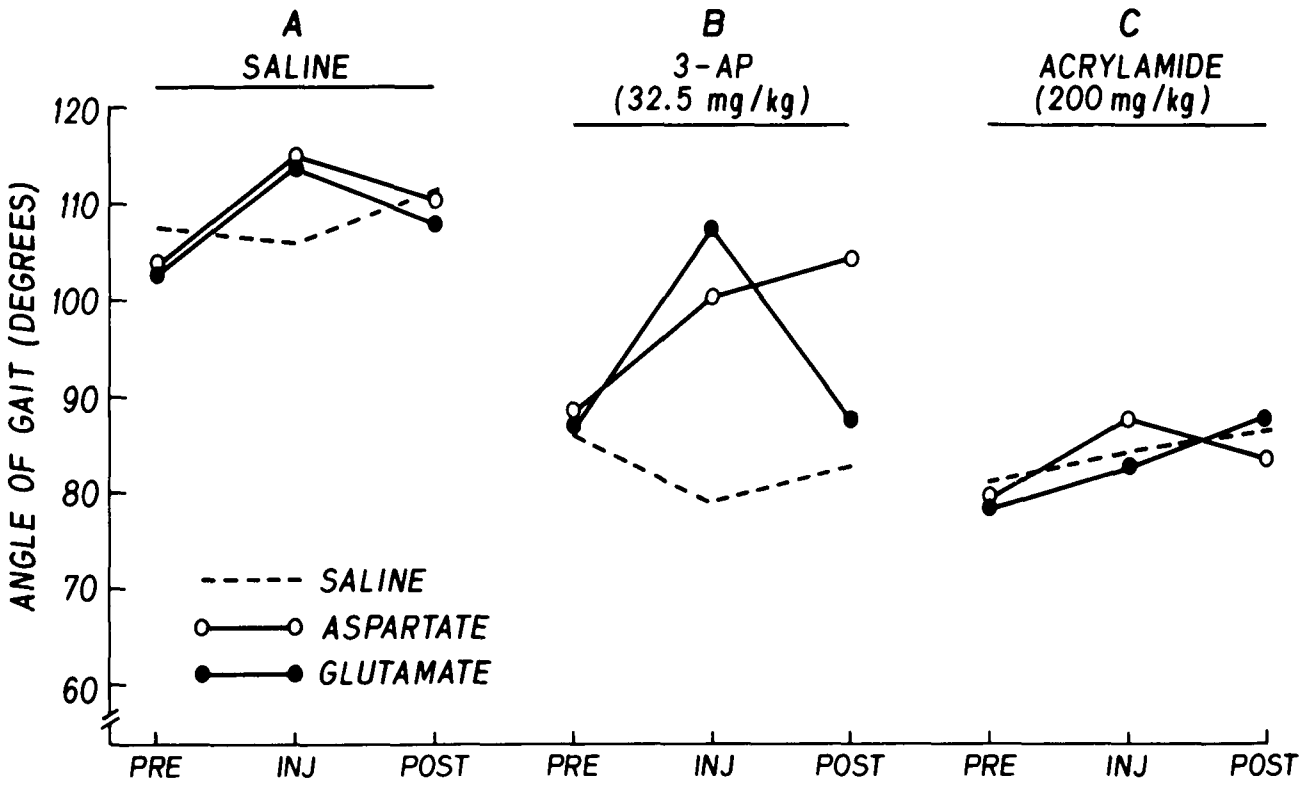

Figure 1 — Mean gait angles (in degrees) presented as a function of the various treatments of this study (Panel C). Data obtained with control (Panel A) and 3-AP treated animals (Panel B) were taken from our previous report (De Michele et al, 1980).

(Panel C) where mean gait angles obtained under the various conditions are presented. For comparison purposes, results from our previous report with control and 3-AP treated animals, are also included in the figure (Panels A and B).

DISCUSSION

A cumulative dose of 200 m/kg acrylamide induced in the animals a clear ataxic gait characterized by a decreased angle of steps. The decrement in step angles was of the same magnitude as that seen with 3-AP (figure 1). As can be seen in the figure, acrylamide induced ataxia was not modified by administration of glutamate or aspartate. These negative results confer specificity to the reported corrective influence of these amino acids on the ataxic gaits induced by 3-AP (De Michele, 1980). It thus appears that glutamate and aspartate can influence cerebellar but not peripheral ataxias in animals.

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