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ORIGINAL ARTICLE

Contribution of hippocampal area CA1 to acetone cyanohydrin-induced loss of motor coordination in rats☆

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KEYWORDS
Cassava;
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Abstract
Introduction: Some vegetable foodstuffs contain toxic compounds that, when consumed, favour the development of certain diseases. Cassava (*Manihot esculenta* Crantz) is an important food source, but it contains cyanogenic glucosides (linamarin and lotaustralin) that have been associated with the development of tropical ataxic neuropathy and konzo. In rats, intraperitoneal administration of acetone cyanohydrin (a metabolite of linamarin) produces neurological disorders and neuronal damage in the hippocampus. However, it is unknown whether hippocampal area CA1 plays a role in neurological disorders associated with acetone cyanohydrin.
Method: A total of 32 male Wistar rats 3 months old were assigned to 4 groups ($n = 8$ per group) as follows: vehicle (1 μl physiological saline), and 3 groups with acetone cyanohydrin (1 μl of 10, 15, and 20 mM solution, respectively). The substances were microinjected intrahippocampally every 24 hours for 7 consecutive days, and their effects on locomotor activity, rota-rod and swim tests were assessed daily. On the fifth day post-treatment, rats underwent further assessment with behavioural tests to identify or rule out permanent damage induced by acetone cyanohydrin.
Results: Microinjection of acetone cyanohydrin 20 mM resulted in hyperactivity, motor impairment, and reduced exploration from the third day of treatment. All concentrations of acetone cyanohydrin produced rotational behaviour in the swim test from the first day of microinjection.

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Conclusion: The hippocampal area CA1 is involved in motor alterations induced by microinjection of acetone cyanohydrin, as has been reported for other cassava compounds.

PALABRAS CLAVE
Yuca;
Acetonacianohidrina;
Neuropatía;
Conducta de giro;
Incoordinación motriz

Participación del área CA1 del hipocampo en la incoordinación motora inducida por acetonacianohidrina en la rata

Resumen
Introducción: Algunos vegetales destinados a la alimentación contienen compuestos tóxicos que, al ser consumidos, predisponen al desarrollo de algunas enfermedades. La yuca *(Manihot esculenta* Crantz) es una fuente importante de alimento, pero contiene glucósidos cianogénicos (linamarina y lotaustralina) que han sido asociados con el desarrollo de la neuropatía atáxica tropical y el konzo. En la rata, la administración intraperitoneal de acetonacianohidrina (un metabolito de la linamarina) produce alteraciones neurológicas y daño neuronal en el hipocampo. No obstante, se desconoce si el área CA1 del hipocampo participa en las alteraciones neurológicas asociadas a la acetonacianohidrina.
Método: Treinta y dos ratas macho Wistar de 3 meses de edad fueron destinadas a 4 grupos (n = 8 cada grupo): vehículo (1 de solución salina fisiológica) y 3 grupos con acetonacianohidrina (1 de solución 10, 15 y 20 mM). Las sustancias fueron microinyectadas intrahipocampalmente durante 7 días consecutivos (cada 24 h); los efectos fueron evaluados diariamente en las pruebas de actividad locomotora, rota-rod y nado. Al quinto día postratamiento se evaluaron nuevamente en las pruebas conductuales para identificar o descartar la permanencia del daño inducido por la acetonacianohidrina.
Resultados: La microinyección de acetonacianohidrina 20 mM produjo hiperactividad, incoordinación motora y reducción de la exploración a partir del tercer día del tratamiento. En la prueba de nado, todas las concentraciones de acetonacianohidrina produjeron la conducta de giro desde el primer día de microinyección.
Conclusión: El área CA1 del hipocampo participa en las alteraciones motoras inducidas por la microinyección de acetonacianohidrina, como ha sido reportado para otros compuestos de la yuca.

Introduction

Various plant foods regarded as daily staples in some parts of the world contain compounds that can have a toxic effect under certain conditions. Under normal conditions, these foodstuffs are processed properly and are safe to consume; however, when they have not been prepared correctly, the toxic compounds that remain may cause illness, including different central nervous system diseases.[1] One of these foodstuffs is manioc root or cassava (*Manihot esculenta* Crantz), which is a good source of energy. The root and the above-ground parts of the cassava plant contain cyanogenic compounds (linamarin and lotaustralin); hydrolisation of these compounds via the linamarase enzyme produces glucose and acetone cyanohydrin, which in turn decomposes into acetone and hydrogen cyanide, a neurotoxin.[2]

Earlier studies reported that rats treated with juice from cassava root (equivalent to 0.30 mg/2 mL of linamarin) developed hyperactivity and loss of motor coordination,[3] as well as a reduction in the number of neurons in hippocampal area CA1.[4] These studies point to the role of the hippocampus in the motor impairment caused by cassava consumption, and probably also in the aetiology of such neurological diseases as konzo and tropical ataxic neuropathy among cassava consumers.[4] Linamarin microinjections to the hippocampus (CA1) elicit hyperactivity and loss of motor coordination in rats, manifesting as higher numbers of crossed squares in the open field test, shorter latency to fall on the rotarod test, and spinning behaviour on the swimming test.[5] Aside from these findings, we do not yet know whether other compounds in cassava, such as acetone cyanohydrin, may also impair coordination and motor activity when delivered to the hippocampus by microinjection. We attempt to answer this question by studying how intrahippocampal microinjections of acetone cyanohydrin affect behaviour in Wistar rats, evaluated using locomotor function, rotarod, and swimming tests.