Behavioural Brain Research 313 (2016) 53–57

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Short communication

Aberrant self-grooming as early marker of motor dysfunction in a rat model of Huntington's disease

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HIGHLIGHTS

- We compare self-grooming behaviour of Quinolinic acid- and Sham-lesioned rats 3 weeks post-lesion.
- Quinolinic acid- rats show shorter latency to groom and increased self-grooming compared to Sham rats.
- Quinolinic acid- rats exhibit altered sequence in their grooming pattern compared to Sham rats.
- Self-grooming may be used as early behavioural marker of striatal damage in experimental models of Huntington's disease.

ARTICLE INFO

Article history:
Received 23 May 2016
Received in revised form 27 June 2016
Accepted 29 June 2016
Available online 30 June 2016

Keywords:
Huntington's disease
Basal ganglia disorder
Motor disease
Self grooming

ABSTRACT

In the study of neurodegenerative diseases, rodent models provide experimentally accessible systems to study multiple pathogenetic aspects. The identification of early and robust behavioural changes is crucial to monitoring disease progression and testing potential therapeutic strategies in animals. Consistent experimental data support the translational value of rodent self-grooming as index of disturbed motor functions and perseverative behaviour patterns in different rodent models of brain disorders. Huntington's disease (HD) is a progressive neurodegenerative disorder, characterized by severe degeneration of basal ganglia, cognitive and psychiatric impairments and motor abnormalities. In the rat species, intrastriatal injection of the excitotoxin quinolinic acid (QA) mimics some of the neuroanatomical and behavioural changes found in HD, including the loss of GABAergic neurons and the appearance of motor and cognitive deficits.

We show here that striatal damage induced by unilateral QA injection in dorsal striatum of rats triggers aberrant grooming behaviour as early as three weeks post-lesion in absence of other motor impairments: specifically, both quantitative (frequency and duration) and qualitative (the sequential pattern of movements) features of self-grooming behaviour were significantly altered in QA-lesioned rats placed in either the elevated plus-maze and the open-field.

The consistent abnormalities in self-grooming recorded in two different experimental contexts support the use of this behavioural marker in rodent models of striatal damage such as HD, to assess the potential effects of drug and cell replacement therapy in the early stage of disease.

1. Introduction

Huntington's disease (HD) is an inherited neurodegenerative disorder, characterized by cognitive and psychiatric impairments and motor disturbances. The motor dysfunction is primarily associated with degeneration of GABA medium spiny neurons (MSN) in the striatum due to abnormal expansion of CAG repeats within the gene encoding huntingtin. In addition to chorea, a dance-like involuntary movement, deficits in motor function include also impairment of voluntary motor function [1].

In rodents, intrastriatal injection of the excitotoxin quinolinic acid (QA) mimics some of the neuroanatomical changes found in HD, including the loss of GABAergic neurons' projections with a relative preservation of interneurons [2]. This lesional model has

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http://dx.doi.org/10.1016/j.bbr.2016.06.058
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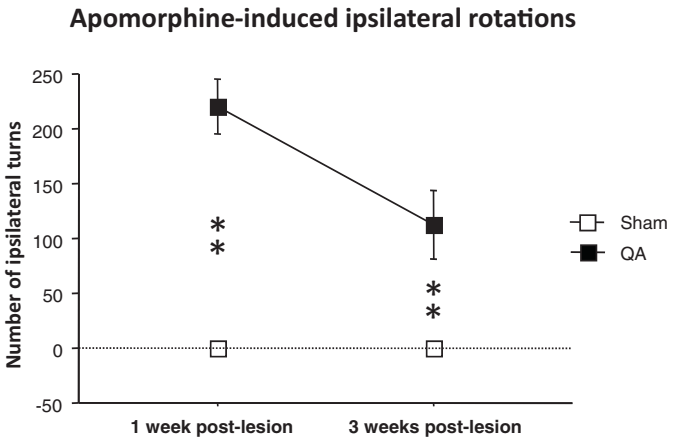

Fig. 1. QA rats exhibited a significant increase in ipsilateral rotational turns compared to Sham rats both 1 and 3 weeks post-lesion. N = 10 rats in each group. Data are represented as mean ± SEM. $^{**}p < 0.01$.

been used in the past years to assess the efficacy of different therapeutic approaches (i.e. drug therapy, enrichment, cell therapy). While bilateral striatal lesions produce marked behavioural changes resembling severe human HD symptoms such as hyperkinesia and cognitive deficits [3], the unilateral lesion produces a milder behavioural phenotype, mainly limited to sensorimotor asymmetry [4]. Thus the unilateral lesion model lends itself to verify the neuroanatomical and functional effects of restorative treatments such as stem cell therapy, as the entity of the brain damage makes it more likely to restore normal function in the damaged circuitry.

In such framework, the identification of consistent anomalies in spontaneous motor patterns relevant to HD in humans is instrumental for monitoring the effects of treatments in the early stages of the disease, before the biochemical changes secondary to the loss of neurons [5].

In a recent review Kalueff and co-workers [6] suggest that rodent self-grooming may be a useful measure of complex patterning of motor activities, of value to translational psychiatry. Aberrant self-grooming (i.e. increase or decrease of self-grooming frequency and duration) has been reported in several rodent models of brain disorders ranging from obsessive compulsive disorders, autism, basal ganglia disorders, HD and Parkinson's disease (PD). Self-grooming is a typical behaviour of the rodents' ethological repertoire, functional to hygiene maintenance and other physiologically important processes. Self-grooming is modulated by novel and stressful conditions [7] as well as by dopaminergic drug administration [8,9], and it is largely controlled by striatal circuitry [10] thus representing a potential functional marker of striatal damage in HD models.

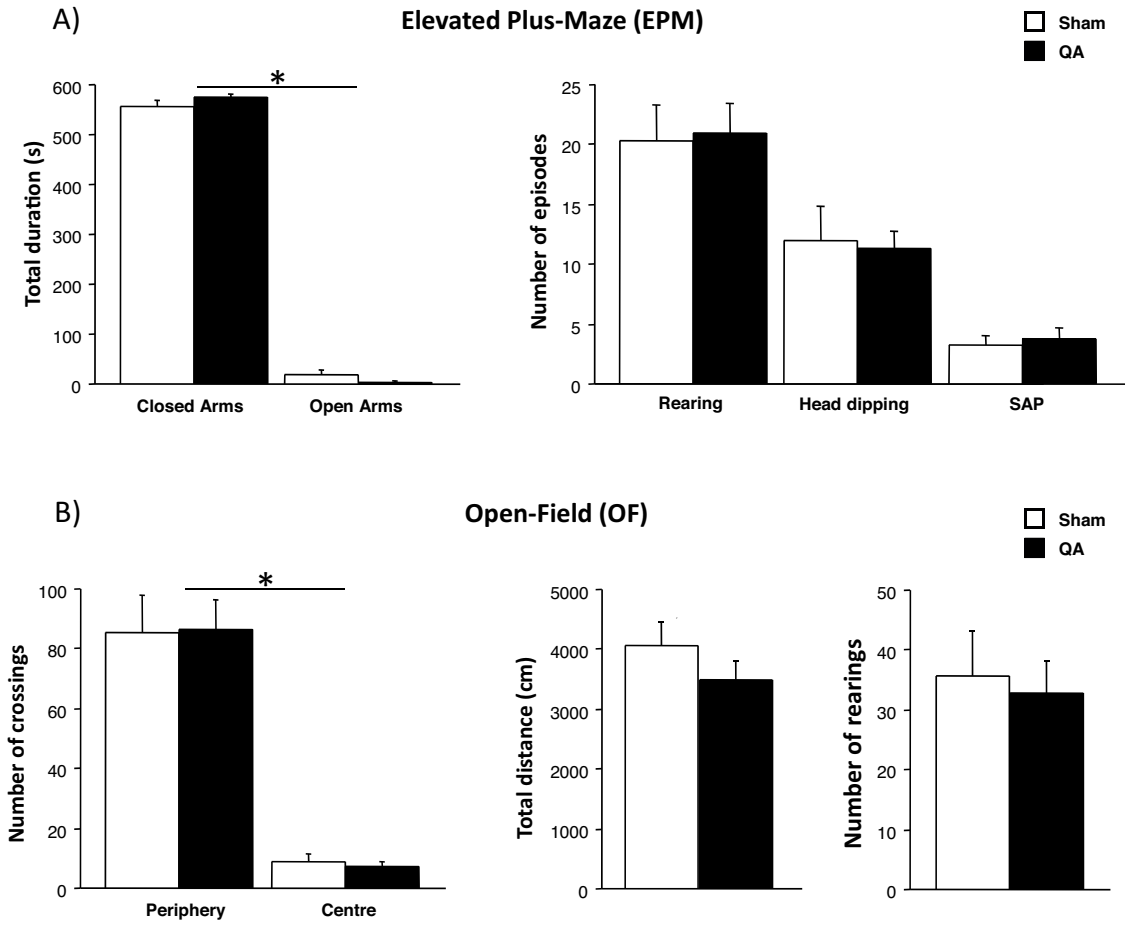

Fig. 2. Behavioural responses displayed by Sham and QA rats in the elevated plus-maze (EPM) and the open-field (OF).
(A) Both Sham and QA rats spent more time in the closed arms and displayed similar levels of explorative behaviours during the 10 min observation period in EPM (SAP = Stretched Attend Postures).
(B) Both Sham and QA rats exhibited a lower crossing frequency in the centre of the OF arena compared to periphery and similar levels of locomotor and explorative activity during the 10 min observation period.
N = 10 rats in each group. Data are represented as mean ± SEM. $^{*}p < 0.05$