



# Social factors affect motor and anxiety behaviors in the animal model of attention-deficit hyperactivity disorders: A housing-style factor



Meng-Li Tsai<sup>a</sup>, Anna Kozłowska<sup>b</sup>, Yu-Sheng Li<sup>a</sup>, Wen-Ling Shen<sup>a</sup>, Andrew Chih Wei Huang<sup>c,\*</sup>

<sup>a</sup> Department of Biomechatronic Engineering, National Ilan University, Yilan, Taiwan

<sup>b</sup> Department of Human Physiology, Faculty of Medical Sciences; University of Warmia and Mazury, Olsztyn, Poland

<sup>c</sup> Department of Psychology, Fo Guang University, Yilan County 26247, Taiwan

## ARTICLE INFO

### Keywords:

Social context  
Housing style  
Motor function  
Anxiety behavior  
Attention-deficit/hyperactivity disorders  
SHR rat

## ABSTRACT

The present study examines whether housing style (e.g., single housing, same-strain-grouped housing, and different-strain-grouped housing) and rat strain (e.g., spontaneous hypertension rats [SHR] and Wistar-Kyoto rats [WKY]) mediate motor function and anxiety behavior in the open field task. From week 4 through week 10 following birth, the rats were measured 30 min for locomotor activity and anxiety once per week in the open field task. The SHR rats exhibited hyperactivity in total distance traveled and movement time to form the animal model of ADHD. The SHR rats spent more time inside the square and crossed the inside-outside line more often than the WKY rats, indicating the SHR rats exhibited less anxiety behavior. The different-strain-grouped housing style (but neither the same-strain-grouped housing style nor the single housing style) decreased total distance traveled and facilitated anxiety behavior. The motor function was negatively correlated with anxiety behavior for SHR rats but not for WKY rats. Housing styles had a negative correlation between motor function and anxiety behavior. The present findings provide some insights regarding how social factors (such as housing style) affect motor function and anxiety behavior related to ADHD in a clinical setting.

## 1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a chronic neurological and neurobehavioral disorder. The characteristics of ADHD include two domains of major symptoms: attention deficit and hyperactivity/impulsive behaviors; these symptoms must be continuously present for at least six months (Austerman, 2015; Rigler et al., 2016). A growing body of studies has shown that many child patients with ADHD first suffered symptoms such as impulsive behaviors while growing up and that these symptoms continued as adults (Archer and Kostrzewa, 2012; Bloemsma et al., 2013). Some research reports estimate the prevalence of ADHD at 3.0–8.9% of children (Caye et al., 2016; Skogli et al., 2013) and 3.5–12.2% of adults (Caye et al., 2016; Matte et al., 2015a; Rigler et al., 2016). In 2013, the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, American Psychiatric Association, 2013) proposed altering the diagnostic criteria of the DSM-IV to change the evaluation method for ADHD patients. For example, the DSM-5 diagnosis of ADHD and the Disruptive Behaviors Work Group has been modified using two major components. First, DSM-5 includes four new impulsivity symptoms. Second, it decreases the number of criteria for the diagnosis of ADHD symptoms (Matte et al., 2015b). In addition, the

DSM-5 raises the age limitation for the onset of ADHD symptoms to 12 years (instead of 7 years). ADHD symptoms are required to occur in at least two settings (Austerman, 2015). These new criteria for diagnosis were thought to increase the prevalence of ADHD by 27.0% for adolescents when comparing DSM-IV to DSM-5 (Matte et al., 2015a).

In the animal model of ADHD, the spontaneous hypertensive rat (SHR) strain has often been used to model the hyperactivity of the ADHD animal model to compare to the control strain, Wistar-Kyoto (WKY) rats (Rommelse et al., 2009; Williams et al., 2009). The SHR and WKY rats were both established from the same paternal, normotensive Wistar stock, and therefore WKY rats are typically used as a control group for the SHR rats (Dela et al., 2013). In the open field test, the SHR rats exhibited more hyperactivity than the control WKY rats. Moreover, the SHR rats were sensitive to dopamine receptors and alpha2 adrenergic receptors (Rommelse et al., 2009). With regard to the pharmacological treatments, the clinical data have shown that either the dopamine reuptake inhibitors methylphenidate (Britton and Bethancourt, 2009) or dopamine releasers amphetamine (Heal et al., 2013) could ameliorate ADHD symptoms. These types of neurotransmitters, such as dopamine and norepinephrine, have also been shown to reduce hyperactivity symptoms in the ADHD animal model. Therefore,

\* Correspondence to: Department of Psychology, Fo Guang University, No. 160, Linwei Rd., Jiaosi Shiang, Yilan County 26247, Taiwan.  
E-mail address: [chweihuang@mail.fgu.edu.tw](mailto:chweihuang@mail.fgu.edu.tw) (A.C.W. Huang).

the present study utilized the SHR strain for testing and WKY rats as a control to examine whether SHR rats could induce hyperactivity in the ADHD animal model.

In addition to attention-deficit and/or hyperactivity symptoms, ADHD patients often present with a variety of comorbidities, such as anxiety disorders, mood disorders, and substance abuse. The ADHD comorbidities for mood disorder, substance use, and anxiety disorder are present in 20.0–30.0%, 12.0–24.0%, and 10.0–49.0% of patients, respectively. Obviously, the comorbidity of anxiety disorders has the widest range (between 10.0% and 40.0%); clinical physicians prescribe different medications for ADHD patients with separate comorbidities (Austerman, 2015). Therefore, patients with ADHD do not absolutely present anxiety disorder. However, many previous studies have shown that anxiety behavior is frequently comorbid with ADHD (Abikoff et al., 2002; Chao et al., 2008; Clarke et al., 2005; Lahey et al., 2007; Owens and Hinshaw, 2013; Skogli et al., 2013). Furthermore, children with ADHD are highly likely to develop anxiety and depression during early adolescence—girls in particular (Lahey et al., 2007). Although many clinical studies have suggested that there is probably a relationship between anxiety and ADHD, little research on the ADHD animal model has been developed to examine whether animals with ADHD symptoms can produce the comorbid anxiety behavior. This issue is investigated in the present study.

To our knowledge, no previous research has used housing style (such as single housing, same-strain-grouped housing, or different-strain-grouped housing) to affect ADHD-induced hyperactivity symptoms. However, the factors of social context and environmental enrichment might ameliorate the impairment of methylphenidate or amphetamine induced in cognitive function and might facilitate drug addiction for ADHD patients (Alvers et al., 2012; Avital et al., 2011; de Carvalho et al., 2010; Perry et al., 2008). For example, a previous study indicated that environmental enrichment decreased the reward impact of methylphenidate for intravenous drug self-administrations in low doses (Alvers et al., 2012). After environmental enrichment interventions, chronic exposure to methylphenidate leads to reduced motor activity. Environmental enrichment can also reduce impairment due to long-term exposure to methylphenidate, thus protecting the brains of ADHD patients (Avital et al., 2011). Environmental enrichment was shown to reduce the effect of motivational properties of ethanol-induced conditioned-place preference and novelty-induced motor activity (de Carvalho et al., 2010). Therefore, the factor of social context is highly associated with ADHD symptoms. Furthermore, the issue of whether social context (such as housing style including single housing, same-strain-grouped housing, or different-strain-grouped housing) can influence ADHD symptoms in motor hyperactivity remains unresolved. Accordingly, the present study concerns whether the different-strain-grouped housing group revealed significantly different motion function and anxiety behavior when compared to single and same-strain-grouped housing rats.

The present study examines the following issues: (A) whether different housing styles can affect the motor activity of SHR rats (relative to that of WKY rats) in the open field task; and (B) whether type of rat and type of housing style can influence motor and anxiety behaviors.

## 2. Materials and methods

### 2.1. Animals

Forty-eight male WKY rats and 48 male SHR rats were purchased from BioLasco Taiwan Co., Ltd. All rats were postnatal day 24 when rats were from BioLasco Taiwan Co., Ltd. Later, all rats were assigned into the appropriate home cages after postnatal day 24. From arrival to postnatal day 24, rats were housed in group of three in a standard home cage. The rats were allowed to habituate to a temperature-controlled colony room for 7 d before being subjected to experiments. Following

habituation, the rats were housed individually or in groups of two, as specified by their group assignments. The plastic home cages were 43 × 21.5 × 21 cm and featured hardwood laboratory bedding (made of Beta Chip). All animals were maintained on a 12-h light-dark cycle with food and water available ad libitum. All the experiments were performed in accordance with the Animal Scientific Procedures Act of 1986, and the present study received the local ethics committee's approval. Efforts were made to minimize the number of animals and their suffering.

### 2.2. Apparatus

The apparatus included a Microsoft Kinect video camera and an open-field plastic box (Ou-Yang et al., 2011). This rectangular plastic box measured 50 cm long × 50 cm wide × 100 cm high. The Microsoft Kinect device was a video camera that could record locomotor activity in all 3 dimensions (3D) for the open field task. The center of the open field task was a square (20 cm × 20 cm) in which the Microsoft Kinect device would measure the motor functions and anxiety behaviors (Pare et al., 2001). Motor functions included total distance traveled and movement time. The time spent inside the central square and the number of times the rats crossed the inside-outside line of the central square would be recorded as the components of the anxiety index. More time spent and more crossings indicated a lower anxiety response (Pare et al., 2001).

### 2.3. Experimental procedure

Following the habituation phase, all of the SHR and WKY (i.e., control) male rats were assigned into six groups: WKY single housing, SHR single housing, WKY same-strain housing, SHR same-strain housing, WKY different-strain housing, and SHR different-strain housing ( $n = 16$  per group). In particular, the WKY different-strain group and the SHR different-strain group were designed with one SHR rat and one WKY rat in each cage. A total of 8 cages were used for the WKY and SHR different-strain groups. All the rats received locomotion and anxiety tests once per week (for a total of 7 trials from week 4 through week 10) after birth and were monitored for the open field task using the Microsoft Kinect device during the testing phase. The behavioral testing phase was performed for 30 min for each trial. All the rats' motor function, anxiety behavior, and health condition were measured. For motor function, total distance traveled and movement time were assessed. For anxiety behavior, the time spent time in the center and the number of inside-outside crossings were measured. Health condition was measured once per week based on each rat's quantity of feces and weight.

### 2.4. Statistics

To verify the main effects of strain and housing style and the interaction of strain and housing style, a 2 × 3 × 7 mixed three-way (strain vs. housing style vs. week) analysis of variance (ANOVA) was used to analyze total distance traveled, movement time, time spent in the center square, number of inside-outside crossings, feces quantity, and weight. Furthermore, a two-way ANOVA (strain vs. housing style) was used to analyze the factors of strain and housing style, as well as the interaction of strain and housing style in terms of the same measurements. Pearson correlation tests were performed to compare motor function and anxiety behavior for the different strain and different housing-style conditions. The correlation test could offer extra information to shed light on the relationship between locomotion and anxiety. Values of  $p < 0.05$  were considered statistically significant.

Download English Version:

<https://daneshyari.com/en/article/4933152>

Download Persian Version:

<https://daneshyari.com/article/4933152>

[Daneshyari.com](https://daneshyari.com)