New Evaluation Method of Neuropharmacological Drug Based on Automatic Extraction of Animal Behavior Indicators

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ABSTRACT

The success of realizing automatic extraction of animal behavior indicators depends on the accuracy of image recognition models, which is caused by the underdevelopment of deep learning technology in the past. Therefore, powerful deep learning tools are needed to solve this problem. Deep learning tools are now widely used for animal pose tracking and label-free animal pose estimation. However, these computer-related open source solutions are extremely challenging for cross-disciplinary researchers, so it is proposed to combine deep learning pose tracking tools with well-established medical index system algorithms. A new method for neuropharmaceutical evaluation based on automatic extraction of animal behavior is proposed. By building a simple and powerful automatic high-throughput index extraction system, competitive performance results are obtained in terms of accuracy, sensitivity, processing time. of the identification system. Therefore, obtaining a high-throughput system with high precision and low latency and establishing a scientific automated medical index extraction system will help to achieve behavioral high-throughput analysis.

CCS CONCEPTS

• **Computing methodologies** → Artificial intelligence; Computer vision; Computer vision problems; Interest point and salient region detections.

KEYWORDS

Image Recognition, Animal Behavior, Neuropharmaceutical

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1 INTRODUCTION

The current research and development of drugs related to neurological diseases has a series of problems with long cycles and high costs [1]. Therefore, the provision of powerful technologies for the research and development of drugs for neurological diseases, as well as the early accurate diagnosis of diseases, for medical intervention and treatment and rehabilitation evaluation is an urgent need to solve the problem.

In behavioral science, commercial solutions mostly use video tracking or infrared sensors. Such systems enable researchers to perform only semi-high-throughput behavioral analyses [2]. However, commercial solutions are not only expensive, but also lack the ability to customize and evaluate specific behaviors of interest. The biggest problems are that their tracking ability is not ideal, and their sensitivity to measure behavior is poor. Therefore, in behavioral evaluation, manual observation and manual counting are mainly used, and the score of human experts is still the gold standard. However, people often feel very tired when doing some repetitive work, and there are a series of problems such as strong subjectivity, low index accuracy and experimental efficiency, which often lead to false negatives or false positives in experimental results, which greatly limits behavioral experiments. Application in the evaluation of drug toxicity and efficacy.

In recent years, significant progress in deep learning has made animal motion tracking possible, providing an important technical tool for the automatic kinematic analysis of motor behavior tasks [3]. It has promoted the development of kinematics analysis in the early warning, auxiliary diagnosis and treatment and rehabilitation evaluation of neurological diseases, which means that the era of behavioral high-throughput analysis has arrived [4]. However, these computer-related analysis methods are extremely challenging for medical researchers. so there is an urgent need to develop an easy-to-use, efficient, and accurate automated behavioral system for the rapid and widespread use of the technology.

2 PRELIMINARIES

2.1 Computer Behavior System

In the past ten years, more and more people are committed to automatically measuring behavior, which is exciting. Both academic open source and commercial hardware/software packages now allow researchers to perform measurements, such as tracking

Table 1: Overview of Deep Learning Tool for Animal

Tool Name	Animal	GUI	3D	Multiple algorithms	Add data	Relrased	Citations
DeepLabCut [10]	Yes	Yes	Yes	Many	Yes	4/2018	1361
DeepPoseKit [11]	No	Yes	No	No	Yes	8/2019	210
DeepBehavior [12]	Yes	No	Yes	No	No	5/2019	56
DeepFly3D [13]	No	Yes	Yes	No	Yes	5/2019	88
OpenPose [14]	Yes	Yes	Yes	No	Yes	7/2019	654
Alpha-pose [15]	Human	No	No	No	Yes	2/2018	1051
Anipose [16]	Human	No	No	No	No	7/2019	645

rodent trajectories in arenas [5] and measurement freezes in fear adjustment experiments [6]. These tools are valuable to the pharmaceutical industry because they allow high-throughput screening of drugs for neurological or neuropsychiatric diseases. Due to the inherent difficulties of building automated systems, most of this work focuses on measuring limited but well-defined behaviors. However, a machine or software created to measure a set of predefined actions will not be able to display new actions or new ways of performing known actions.

2.2 Trajectory tracking

Tracking means calculating the trajectory. First, the animals are detected, that is, the animals are identified and distinguished in each frame of the video, and the position of the animals is measured. In addition, you can also measure other parameters, such as the direction of the body, limbs, and other limbs; this richer body shape feature is usually called ”posture”, and the position and posture of each animal are connected frame by frame. To obtain a trajectory describing its movement in time. In fact, due to the lack of standardization, the proliferation of automatic video tracking software has also created its own problems. Tracking software that is universal in a variety of environments and organisms is an important step to solve this problem [7].

2.3 Behavior analysis

Behavior analysis, its ultimate goal is to evaluate ”activity”, that is, a large-scale behavioral pattern (attack, courtship) composed of different behaviors. This analysis includes at least computational behavior graphs [8]. Which describe the frequency of each behavior and the probability that a given behavior will subsequently occur in another behavior. More sophisticated levels of analysis include the development of models of how animals make decisions and control their behavior based on their internal states and external stimuli [9].

2.4 Overview of Deep Learning Tool for Animal

Over the past decade, there have been many open source deep learning pose tracking tools worthy of our research. They use different neural networks and pose estimation algorithms. The significant progress based on deep learning has made animal motion tracking possible. Table 1 summarizes the different Deep Learning Tool for Animal features.

2.5 Data processing formula of Behavior analysis

Data processing involves a variety of operations and techniques for transforming raw data into meaningful information. Therefore, the key formulations commonly used in this study are outlined as follows.

1) 2D space formula.

$$d = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2} \tag{1}$$

This formula is used to find the distance between any two points on a coordinate plane or x-y plane*;* If the coordinates of two points P and Q are such that, (x_1, 0) and (x_2, 0), the distance between d will be given by, d = $|x^2 - x^1|$.

2) 3D space formula.

Let us consider two points A(x_1, y_1, z_1) and B(x_2, y_2, z_2) in 3d space. Then, the distance formula for these two points is given by;

$$d = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2} \tag{2}$$

Distance of any point C(x, y, z) in space from origin O(0,0,0), is given by, $d = \sqrt{x^2 + y^2 + z^2}$

3) Angle between two 2D vectors.

$$angle = arccos \frac{(x_a \times x_b + y_a \times y_b)}{\left(\sqrt{(x_a^2 + y_a^2)} \times \sqrt{\left(x_b^2 + y_b^2\right)}\right.}, \quad a = (x_a, y_a), b = (x_b, y_b) \tag{3}$$

4) Angle between two 3D vectors.

$$angle = arccos \frac{(x_a \times x_b + y_a \times y_b + z_a \times z_b)}{\left(\sqrt{(x_a^2 + y_a^2 + z_a^2)} \times \sqrt{\left(x_b^2 + y_b^2 + z_a^2\right)}\right.}, \quad a = (x_a, y_a, z_a), b = (x_b, y_b, z_b) \tag{4}$$

3 METHODS

This section presents a scheme proposed in this paper based on a deep learning pose tracking tool combined with a well-established medical indexing algorithm. The program uses Deeplabcut to build a tracking model to ensure the accuracy of tracking. The medical index algorithm is to ensure the conversion of animal posture coordinates into scientific medical indicators. In order to obtain high-precision, low-latency, high-throughput animal behavior analysis results. The steps for establishment of animal movement model are:

- Step1: Extract frames from the video

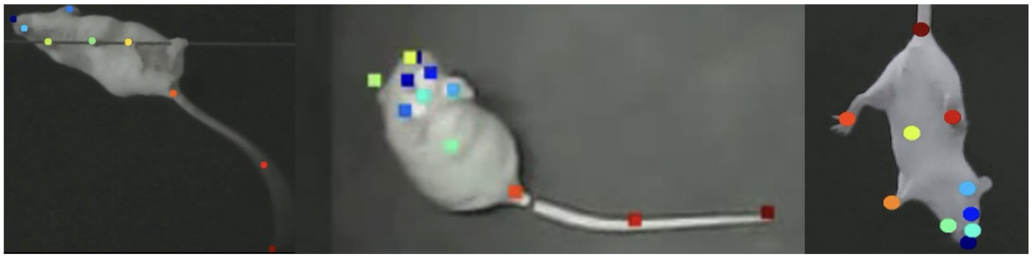

Figure 1: Animal image tagging dataset

A good training set data should contain enough high frame rate data to obtain complete animal behavior to ensure that it can reflect the behavioral diversity of animal postures. We use a single high frame rate industrial camera to take top-level shots of the experiment and collect different videos for different animal individuals (for example white or black mice), lighting conditions, and backgrounds. as well as we will choose animal videos with more behaviors from which to extract images while keeping the frame size small to prevent the training and analysis from taking too long.

- Step2: Label frames

Deep learning based animal tracking is highly dependent on high quality marker images. This suggests that marker images that are highly usable and reflect the animal's movement behaviour should be used. If body parts in still images cannot be reliably identified due to video quality (i.e. body parts are obscured due to extensive motion blur), then we want to ensure consistent image quality. Figure 1. shows the Animal image tagging data.

After ensuring that the labelled images are reliable, the 12 joint points of the animal (tip of nose, eyes, ears, head, limbs, centre of torso, base of tail) will be labelled, laying the foundation for the creation of the dataset. Annotation of a large amount of image data is completed to create data set. The rat behaviour module includes: autonomous activity module, locomotor ability module, mood analysis module and cognitive ability module. In addition, there are almost a hundred behaviours: different postures, different sizes and different moments.

It is important to use the large amount of high-quality image data from different videos to accurately label the body parts of the animals and to ensure that there is agreement on the labeling criteria before starting to label, thus ensuring that the same position is labeled for any body part (e.g. the head of a rat).

- Step3: Create training dataset

In order to create a robust network that can be reused in the laboratory, a good training dataset should reflect the diversity of behaviors in terms of poses, brightness conditions, background conditions, animal identities.

So our 200 videos were manually labeled by 7 experimenters, including 150 mice (110 Kunming mice, and 40 C57 mice). In addition to differences, there are differences in their age (young, middle-aged, and aged), groups (normal model, depression model, depression model-administration treatment model, dbdb diabetes model, alcohol model), and the video shooting environment Diversified (ambient brightness, distance from the camera, shooting angle, dimensions are different).

To optimize the training set, we used manual cross-checking to double-check all marker images, thus ensuring that all markers were in the actual position of the animal's body parts. For obscured body parts and for any unusable images, we removed them from the dataset.

- Step4: Train network

By testing different neural network algorithms (ResNet, ResNeXt, AmoebaNet, MobileNet, ShuffleNet, SqueezeNet, Xception, MobileNetV2.), the optimal algorithm is selected and applied to this research.

By optimizing video parameters (video frame rate, bit rate) to increase speed, optimizing mark pictures, etc., a trade-off between speed and accuracy is made.

Use high-performance GPU clusters to train network. For each labeled video, the other videos were used to train the neural network. The model is then cross-validated on a single video not included in the training set.

- Step5: Evaluate network

It is important to evaluate the performance of the trained network. This performance is measured by computing the mean average Euclidean error (MAE; which is proportional to the average root mean square error) between the manual labels and the ones predicted. This helps exclude occluded body parts.

If the model evaluates poorly, we assess whether more data is needed, and if so add more videos of animal behaviour to increase the labelled data and train again. In cases where there is not enough data, we artificially extend the training set by rotating or rescaling the image into a new image, using a more powerful and accurate model.

- Step6: Analyze video

Use the toolbox to analyze the video to derive the x- and y-coordinates of the marked feature positions, and use interpolation to fill in the parts where the feature positions are not correctly identified, eliminating errors caused by false occlusions or other factors to improve accuracy.

Processing of Behavior analysis:

It is extremely challenging to convert the raw animal motion data from image recognition into medical behavioral assessable data. The focus is on how to convert raw data into medical indicators using algorithms or formulas that can be processed by computers. These data are used to illustrate the occurrence and development of diseases or the efficacy and toxicity of drugs. So we need to find the correlation in the data and build the correlation

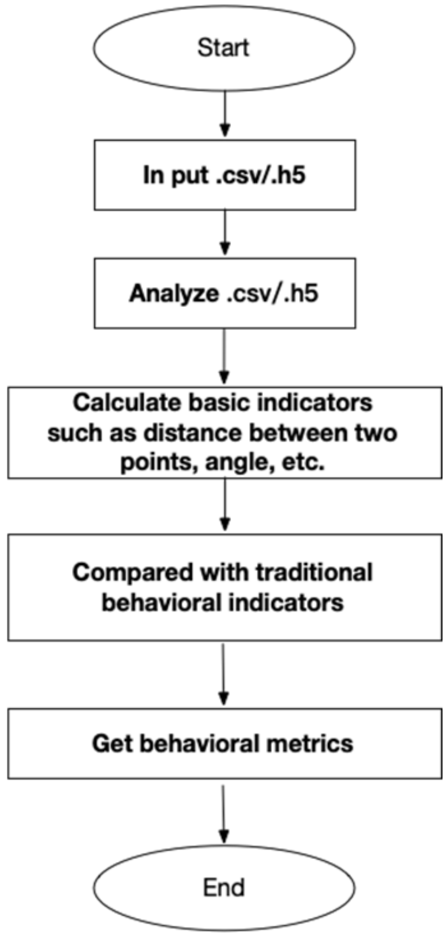

Figure 2: Medical Index Algorithm

function to make it possible to evaluate the loss of function. Figure 2 shows the flowchart of the medical index algorithm. We use deep learning tools for animal behaviour tracking to provide raw data for analysing animal behaviour. In this section, it is imminent to help researchers analyse animal behaviour in a high-throughput manner. To achieve this, we have developed an algorithmic program using Python that can load and process CSV files. The program will analyze and process animal behavior data generated using the model using traditional behavioral metrics. so that the animal behaviour tracking data obtained can be used to achieve an accuracy close to that of human experts when scoring behaviour related to complex behavioural studies. By quantitatively analysing the trajectories of the animal's body parts. We can calculate movement distance, movement time, movement acceleration, angular information and their relationship to time, providing the basis for detailed animal behaviour assessment, and this basic data has a wide range of application scenarios. Unsupervised methods such as clustering methods, association rules, dimensionality reduction or autoencoders allow the extraction of common 'movement behaviours' such as turning, running and standing up. Supervised methods, such as scikit-learn, allow for the prediction of custom labels, such as 'climbing a wall' or 'stationary'. By using these methods flexibly we can automatically analyse animal behaviour in various scenarios (open field, elevated plus maze, forced swim test) and give results.

- Step1: Import the animal pose CSV file generated by the animal model.
- Step2: Calculate basic indicators such as distance between two points, angle, etc.
- Step3: Compared with traditional behavioral indicators.
- Step4: Get behavioral metrics.

4 CONCLUSION

This study proposes artificial intelligence techniques to provide new methods for neuropharmaceutical evaluation by tracking animal behavior and subsequent behavioral analysis for high-throughput animal behavior analysis. The proposed method enables researchers without programming experience to fully grasp the behavioral information of animals. By increasing the complexity of animal behavior evaluation methods and overcoming the shortcomings of human expert evaluation methods, we break through the limitations of animal behavior evaluation in drug screening and neuroscience research.

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