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Three-dimensional rodent motion analysis and neurodegenerative disorders

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Abstract

Background—Three-dimensional (3D) motion analysis is established in investigating, human pathological motion. In the field of gait, its use results in the objective identification of primary, and secondary causes of deviations, many current interventions are the result of pre- and post-testing, and it was shown recently that it can result in decreased number of surgeries and overall cost of care. Consequently, recent attempts have implemented 3D motion analysis using rat models to study, parkinsonism. However, to-date, a 3D user friendly analytical approach using rodent models to, identify etiologies of age-related motor impairment and accompanying pathologies has not been, implemented.

New method—We have developed and presented all aspects of a 3D, three body-segment rodent model, to analyze motions of the lower, upper and head segments between rodents of parkinsonism-type and, normal aging during free walking. Our model does not require transformation matrices to describe the, position of each body-segment. Because body-segment positions are not considered to consist of three, rotations about the laboratory axes, the rotations are not sequence dependent.

Results—Each body-segment demonstrated distinct 3D movement patterns. The parkinsonism-type, genotype walked slower with less range of motion, similarly to patients with parkinsonism.

Comparison with existing methods—This is the first model considering the rodent's body as three, distinct segments. To the best of our knowledge, it is the first model to ever consider and report the 3D, head motion patterns.

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Conclusions—This novel approach will allow unbiased analysis of spontaneous locomotion in mouse, models of parkinsonism or normal aging.

Keywords

Movement disorders; Parkinson's disease; Aging; Motion analysis; Movement function; Kinematics

1. Introduction

The ability to perform the function of walking safely and smoothly requires the integration of intact visual, vestibular, proprioceptive and musculoskeletal systems to allow the appropriate neuromechanical processes to maintain postural control. However, declines in all systems and all three stages of processing, including sensory processing, sensorimotor integration and motor output, and, therefore, balance, are found with aging (Light, 1990; Shumway-Cook and Woollacott, 2007). Because the integration of processed input and motor output takes place at the cortical level, increasing evidence from clinical research and practice, epidemiological studies, and clinical trials shows that gait and cognition, or executive function, are interrelated in terms of reduced function in older adults (Montero-Odasso et al., 2012). Recent studies suggest that early changes in gait and gait stability may predict deficiencies in attention and working memory, and possibly also predicting future loss of movement function paralleled with cognitive impairment eventually leading to dementia (for review, see Montero-Odasso et al., 2012). Because of this connection between aging-related movement dysfunction and cognitive impairment, quantitative gait and movement assessment may be utilized as a sensitive and measurable tool for determining potential risk for frailty and progression to dementia in older adults (Karakostas et al., 2013).

Parkinson's disease (PD) is one of the aging-related neurological disorders that afflicts an increasing number of individuals in Western cultures. If the wider complex of extrapyramidal symptoms referred to as parkinsonian syndrome (PS) is included, the incidence is near 50% of the population over 80 years of age (Bennett et al., 1996). Currently there are no treatment paradigms that will stem the degenerative aspect of the disease, and the etiology is still unknown, although it is well recognized that age is the number one risk factor for PD (Eggers, 2009). To date, the most accurate measurement scales for PD and other movement disorders have been qualitative assessment scales, such as the Hoehn and Yahr scale, or the more recently adopted UPDRS scale (Universal Parkinson's Disease Rating Scale) (Martinez-Martin, 2013). These movement assessment scales are objective and do not provide a quantitative and unbiased analysis of movement. Although these scales have been developed specifically to provide low inter-rater variability, the outcome is subjective and to a great extent depends on the person performing the test (Schrag et al., 2009). It has been suggested that a comprehensive evaluation of all different symptoms of movement disorders of aging is possible using a combination of measures completed by health professionals, patients and/or caregivers. However, until recently, no quantitative assessment of movement using motion capture systems has been employed in patients.

A few research groups have recently evaluated novel quantitative gait and motion analysis systems in order to measure motor dysfunction associated with movement disorders and effects of drug treatment or disease progression. For example, Das et al. (2011) performed full-body motion capture of PD patients with deep brain stimulator off-drugs and with stimulators on and off (Das et al., 2011). Their results suggested that their motion capture system was capable of measuring distinctive differences between mild and severe symptoms of the disease. Data obtained from the Support Vector Machine (SVM) classifier used demonstrated discrimination of mild vs. severe symptoms with an average accuracy of approximately 90%. Thus, their data supported the notion that motion capture and related technology could potentially be an accurate, reliable and effective tool for tracking progression of PD, as well as potential beneficial effects of surgical or pharmaceutical treatment paradigms. In other studies, investigators have shown validity of optical capture-related measurements for either tremor (Rigas et al., 2009) or gait (Esser et al., 2012) in patients with movement disorders, again showing that novel methods for motion capture can be utilized for quantification. In Esser et al. (2012), investigators used both inertial measurement units (IMU) or optical motion capture systems (OMCS) to objectively measure gait in patients with Parkinson's disease. They found no differences between the OMCS and IMU in terms of stride length, step time or walking speed, suggesting that these optimized measurement systems could be utilized to objectively evaluate gait in this patient group. These recently developed methods can enhance the accuracy of research studies and provide better predictions of disease progression. However, since most drug trials for PD involve pre-assessment in models of the disease, translatable and accurate motion capture methods also have to be developed for mouse and rat models.

The use of instrumented motion analysis with cameras for the purpose of studying different pathologies and respective treatment paradigms on rats or rodents, such as for spinal cord injury, is well established (Bouyer, 2005; Jung et al., 2009; Leblond et al., 2003; Snigdha et al., 2011). Even though most studies implement video-based motion capture systems because of their processing flexibility, OMCS have an advantage with respect to the speed of processing. However, whether a video-based or an optoelectronic camera motion capture system is used, the data collection process and system output is the same. Markers need to be placed on selected body landmarks which are tracked by the cameras of the system, each camera capturing two-dimensional (2D) images of each marker. When more than one camera is used and the system software implements the appropriate algorithms, then the three-dimensional (3D) coordinates of each marker in space are produced. However, for this information to have any functional meaning, there needs to exist a kinematic model implementing the correct transfer functions to transform the 3D marker coordinates to the position, and ultimately the motion, of the body segment in 3D space. For example, if a body is modeled as a line, even though one can have the 3D coordinates of the markers representing that body, the kinematic information that can be obtained will be motion in only two of the three planes of movement (Thota et al., 2005).

Similar problems regarding the identification of ways to express angles in 3D space for the analysis of human motion have existed in the past for engineers. The most common approach used to be to establish a fixed global or laboratory coordinate system and measure rotations about these axes. However, such an approach does not produce a unique set of

angles that can describe the orientation of the body because the values can change based on the order of rotations. In other words, the angles are sequence-dependent. Attempts to circumvent this problem have been implemented, at the expense, however, of the anatomical interpretation of the results (Kinzel et al., 1972; Patriarco et al., 1981; Soutas-Little and Inman, 1999). Euler (1776) with his study of the motion of the spinning top provided insights to this problem, which later were implemented in the description and quantification of human movement (Grood and Suntay, 1983). While the position of the spinning top could be completely described by a transformation matrix between the coordinates of the laboratory and top systems, if the rotational position is considered to be made up of three rotations about the laboratory axes, then the amounts of these rotations are sequence dependent. However, Euler showed that the position and rotations can be measured about one axis in each system and the third rotation measured about a line of nodes. These angles do not have to be expressed in a form of a transformation matrix while at the same time their power is underlined by their ability to uniquely describe the position of the object. In engineering, these angles are referred to as the yaw, pitch and roll (Goldstein, 1960).

To the best of our knowledge, our group was the first to report on the feasibility of using an OMCS to study aging-related changes on a mouse while walking (Karakostas et al., 2008). Madete et al. (2010) also utilized an OMCS to investigate movement dysfunction during gait on different types of beams, of rats with a unilateral 6-hydroxydopamine (6-OHDA) lesion, a common model for PD. The conclusion was that marker-based motion capture could provide a novel approach to quantifying temporal-spatial gait parameters for rat models of PD (Madete et al., 2010). This group also followed up with another manuscript, in which they used the same marker protocol to investigate the postural adaptations of the body of the rats as a function of dopamine depletion (Madete et al., 2011). While to describe the postural adjustments of the body, they used Euler angles, they provided no information with respect to the definition of their axes of motion. Furthermore, the body, based on the reported data, was considered as one rigid segment, although careful observation of mouse movement suggests that the motion patterns of the rear body and the front/anterior body may be different. Additionally, no consideration was given to the potential contribution of the head motion relative to the adaptive behavior of the subjects. Nevertheless, these few studies suggest that motion capture can also be utilized to assess motor dysfunction in rat and, potentially, mouse or rodent models. However, a body model and a subsequent computational kinematic model have not been developed yet for the rodent such that it can distinguish hind or rear body versus anterior body versus head movement, or that is sensitive enough to assess temporal-spatial movement changes, such as velocity, in mouse models of the disease.

Consequently, the overall aim of the current manuscript is to demonstrate a novel model for motion capture in a mouse model of PD, which can be utilized to extrapolate results from mouse PD models to clinical assessment in humans, and validate, for example, drug trial efficacy using “gold standard” animal models. The objectives are to propose a rodent body data collection model, and then propose, construct and implement a kinematic model for the different body-segments of the rodent.

2. Materials and methods

2.1. Subjects/animals

Glial cell line-derived neurotrophic factor is a protein that is essential for the survival and maintenance of substantia nigra dopamine neurons (Mickiewicz and Kordower, 2011). Our group has shown that mice with a partial deletion of the GDNF gene (*Gdnf*^{+/−} mice) exhibit progressive spontaneous locomotor deficits when they are middle-aged (Boger et al., 2010), coupled with loss of dopamine neurons and reduced ability to perform in an accelerated rotorod, a behavioral task for motor learning and coordination (Boger et al., 2010). In the current study, two twelve months old *Gdnf*^{+/−} mice and age-matched wildtype (WT) littermates were anesthetized with isoflurane and 2 mm diameter retro-reflective markers were fixed to their hair via hypoallergenic double-sided tape. For the marker placement, six anatomical landmarks were used, including the anterior rim of the pelvis and the greater tubercle bilaterally (RR, RL, FR, FL respectively), the middle of the back at the level of L4 (S), and the top of the head (T_A) (see Fig. 1). Based on this marker placement, the orientation and motion in 3-dimensional space of each body segment of the mouse (anterior and posterior bodies, and head) was determined.

2.2. Experimental design/data collection

A 6-camera VICON optical capture system (Vicon Motion Systems Inc., Lake Forest, CA) using MX13 cameras with 1.3 megapixel resolution, maximum absolute error of less than 0.5 mm and filming at 240 Hz monitored the position and movement of each marker in three-dimensional space. The rodents were allowed to move freely in a constrained walkway that was 2 feet long, ½ foot wide and was contained by 5 inches tall walls. They were positioned at the beginning of the walkway manually at the same starting location and they were allowed to walk at a self-selected pace to the end of the walkway. A calibration trial was performed to establish the global, laboratory, coordinate system, its origin, and the three-dimensional volume within which the rodent moved. A kinematic model was implemented in a custom computer program. The model ultimately determined the relative angles of the anterior and posterior body-segments and the head assessing flexion/extension in the sagittal plane of motion, tilting or body side depression in the frontal plane and rotation or spin in the transverse plane of motion. The velocity of forward progression was estimated from the marker positioned at L4 on the back.

2.3. Model development

The marker placement configuration was such that two markers on each body segment of the body of the mouse were placed on a medial-lateral direction at the rear and the front bodies while the third marker was placed in the anterior-posterior direction to the other two and half the distance in the medial-lateral direction between them (Fig. 1). For the head body-segment a different marker configuration was implemented due to the challenge of placing markers to define a plane. Consequently, along with the marker at the top of the head, T_A , another marker was defined at the base of the head, B_A , from the two markers placed on the greater tubercles. A third marker, virtual marker, was established based on the height of the head, h_A . The position of this marker was tracked as a function of the T_A marker. The placement of the markers was deliberately such that they all followed anatomical lines. For

example, the medial–lateral line formed by the markers placed at the anterior rim of the pelvis represented an anatomical line about which the posterior body-segment is elevated, extended, or depressed, flexed; the line formed by a point half the distance between the markers placed on the greater tubercles (in the medial–lateral direction) and the marker on the middle of the back at the level of L4 represented an anatomical line about which each side of the of the front body of the mouse was being elevated or depressed. Furthermore, the marker placement allowed the definition of three distinct body-segments, the head (A), the anterior body (B), and the posterior body (C). These marker-triads also formed the foundation for the formation of each body-segment coordinate system.

For the rear and the front body-segments, the y coordinate of each body-segment was chosen to coincide with the medial–lateral axes of each body-segment. Therefore, the unit vector $\hat{i}_2$ in the y direction is defined by the vector from point RR to the point RL (Fig. 1) and its respective absolute magnitude:

$$\hat{i}_2 = \frac{\vec{RRRL}}{|\vec{RRRL}|} \quad (1)$$

For the rear body-segment a perpendicular coordinate in the z , vertical direction, of the body-segment was then formed from the cross product of the $\hat{i}_2$ unit vector with the vector from point RR to S (Fig. 1):

$$\vec{Q} = \vec{R} \vec{R} S \times \hat{i}_2 \quad \text{where } \hat{i}_3 = \hat{q} = \frac{\vec{Q}}{|\vec{Q}|} \quad (2)$$

The third orthogonal body-segment unit vector in the posterior-anterior direction, x , of the body segment is the cross product of the first two:

$$\hat{i}_1 = \hat{i}_2 \times \hat{i}_3 \quad (3)$$

It is obvious that this body-segment system then is aligned in the anterior-posterior direction to the body-segment, it is aligned in the medial–lateral direction to the body-segment as well as it is aligned to the vertical direction of the body-segment. The body-segment system was established at the geometrical center of the body-segment.

In this manner, local body-segment coordinate systems were formed for the rear body, as explained, the anterior body and the head. However, for the head, the x coordinate was selected to coincide with the posterior-anterior axis of the head with a unit vector $\hat{i}_{1A}$. A perpendicular coordinate with unit vector $\hat{i}_{2A}$ pointing in the medial-lateral direction was formed by:

$$\vec{J} = \hat{i}_{1A} \times \vec{B}_A h_A \quad \text{where } \hat{i}_{2A} = \hat{j} = \frac{\vec{J}}{|\vec{J}|} \quad (4)$$

and the third orthogonal head body-segment unit vector $\hat{i}_{3A}$ is determined by the cross product of the other two (Fig. 1).

The position of each body-segment in space as a function of time, then, was determined in an Eulerian approach (Goldstein, 1960). Euler had suggested the use of two coordinate systems to measure three-dimensional rotations of one rigid body relative to another. One coordinate system was attached to the object and one to the laboratory. Rotations were measured about one axis in each system and the third rotation was measured about a line of nodes, i.e., a mutually perpendicular axis to the other two. With a global reference coordinate system $\hat{I}_1$, $\hat{I}_2$, and $\hat{I}_3$ representing the posterior-anterior direction, medial-lateral and vertical directions respectively, body-segment flexion/extension was defined as rotation about an axis in the $\hat{I}_2$ direction, motion in the transverse plane was defined as rotation about an axis in the $\hat{I}_3$ direction and elevation/depression of the right aspect of the body-segment was defined as rotation about an axis, the line of nodes, the direction of which was defined as:

$$\hat{u}_1 = \frac{\hat{I}_2 \times \hat{I}_3}{|\hat{I}_2 \times \hat{I}_3|} \quad (5)$$

We decided to express extension as positive. Rotation in the transverse plane of the body-segment toward the left with respect to the direction of movement was defined as positive. Rotation in the frontal plane of the body-segment toward the right side was defined as positive, suggesting that depression of the right side of the body-segment was positive.

3. Results

The resulting motion based on the model and the Eulerian approach that was implemented can be seen in Figs. 2–4. The results demonstrated a full walk along the entire walkway and some exploration/motor activity at the end of the walkway. The resulting kinematic ranges of motion along with the linear velocity of each rodent to reach the end of the walkway can be seen in Table 1.

Sagittal plane motion for all body-segments was increased in WT compared to the age-matched *Gdnf*^{+/−} genotype. Frontal plane motion was minimal for the head and front body for both genotypes. Front plane motion, however, did take place in the rear body-segment and it was similar for both groups. The greatest genotype differences observed in the posterior part of the body was for transverse plane motion (Fig. 2C), where the WT exhibited a much greater range of motion than their counterparts. Differences in posterior body movement between the two mouse strains, may suggest a lack of flexibility in the movement of *Gdnf*^{+/−} type compared to the age-matched WT type. With respect to the front body movement, (Fig. 3), genotype differences were observed in the in the sagittal and transverse planes. In fact, motion range differences in the transverse plane were most pronounced between the two mouse strains in the front body-segment, again, suggesting greater front body flexibility for the WT-type. Head movement was also altered in *Gdnf*^{+/−} strain, who exhibited a reduced movement pattern in the sagittal and frontal planes, almost half that of the WT strain. Finally, the velocity to reach the end of the walkway was highest for the WT genotype (Fig. 5), and a greater fluctuation of velocity was observed in this genotype as well.

4. Discussion

The purpose of this paper was to construct, propose and implement a 3D, 3 body-segment rodent body data collection model along with a 3D mathematical model to track and quantify the 3D motion of the rodent's body-segments in order to study neurodegenerative diseases, such as aging and PD. In classical dynamics, one of the goals is to achieve rotational measures which will uniquely locate a rigid body relative to a fixed axis system, such as a laboratory system, and still maintain some physical significance. Measuring, however, rotations about these fixed axes provide rotational amounts which are sequence dependent. In other words, the angular values would change with the order of rotations and, therefore, there would not be a unique set of angles to describe the orientation of the rigid body (Kinzel et al., 1972; Patriarco et al., 1981; Soutas-Little and Inman, 1999). Euler, however, constructed an approach in his study of the motion of the spinning top by which the motion could be described by a set of three angles, the Euler angles, determined by a coordinate system that involved the combination of the laboratory and the spinning top coordinate systems. These angles were not sequence dependent, they did not have to be expressed in a form of a transformation matrix, and they could be considered as rotations in two planes and a rotation about an axis represented by the line of intersection of these two planes called the "lines of nodes" or the "floating axis" (Goldstein, 1960).

Instrumented motion analysis has been using the Eulerian approach for years to describe and objectively quantify human motor behavior at the body-segmental level, such as for walking, reaching, standing sitting, etc. Motion is described in terms of its kinematic characteristics, such as position, velocity and acceleration (linear or angular for each joint) and in terms of its kinetic characteristics, such as joint torques and joint reaction forces. Recently, there have been a number of attempts to implement instrumented motion analysis with rats or mice (Johnson et al., 2012; Madete et al., 2011, 2010) to study pathologies, such as PD or spinal cord injury, because mouse models have the advantage over other animal models of easier identification and experimentation on the genetic mechanisms that affect behavior. However, no group provided a clear description of the mathematical model approach used for the purposes of replication.

Furthermore, while previous approaches for the same purpose treated the body of the rodent as one rigid segment (Madete et al., 2011, 2010), after careful observation of the motion of the rodent's body and knowledge of the human postural responses to perturbation to maintain balance, especially with PD as the underlying pathology (O'Sullivan, 2001), we considered the body as two different body-segments, the rear body-segment and the front body-segment. Furthermore, nowhere in the literature, to the best of our knowledge, the motion of the head of the rodent, or mouse or rat, and irrespective of the objective studied, has been tracked or reported as a 3D body-segment. Our approach, however, treated the rodent's head, and subsequently modeled it, as a distinct 3D body-segment and reported on its individual 3D motion. Our results clearly suggest that there can be pronounced differences in head movement between the two genotypes we studied, showing a reduction in both sagittal and frontal plane movement of the head in the type with reduced GDNF expression (see Fig. 4 and Table 1). We therefore believe that the model presented here

represents a clear improvement over previously published motion capture models for PD-related movement alterations in rodents.

When we consider our results within the context of the information available for humans with PD, our findings agree with the human-related literature. Similar to the to the profoundly reduced walking velocity observed in individuals with PD (Whittle, 2007), the walking velocity output for the WT type was more than twice higher compared to the *Gdnf*^{+/-} genotype as a self-selected walking speed to ambulate the length of the walkway. In addition, there is an abundant body of evidence for humans which shows that with PD one of the characteristics is the decrease of the range of motion of the different body segments and joints, which may further result in impaired balance and body posture (O'Sullivan, 2001; Shumway-Cook and Woollacott, 2007). The results from our study show that mobility in the sagittal plane was higher for the WT genotype for all body-segments. This finding is complemented by the observation that one of the characteristics of PD is the reduced vertical trajectory of the head during walking (Whittle, 2007). In our study the average vertical displacement of the *Gdnf*^{+/-} genotype was approximately half that of the WT type (see Fig. 4). In the transverse plane, mobility was also higher for the WT mouse for the rear and front body-segment. However, with respect to the head, the *Gdnf*^{+/-} mouse demonstrated higher mobility. It may be argued that the WT mouse used sagittal plane motion to explore while reaching the end of the walkway, whereas the *Gdnf*^{+/-} mouse showed preference in the transverse plane in order to explore the environment while walking to the end of the walkway. Such an approach would be most energy cost effective and it would be consistent with the observation that individuals with PD demonstrate decrease in strength (O'Sullivan, 2001). Raising the head vertically against gravity would require more strength. However, demonstration of this preferential behavior as a genotype-related characteristic remains to be shown with further testing. Our model, however, provides this capability, contrary to recently produced motion capture models for rodents.

One aspect of our results that was surprising, was the minimum amount of mobility in the frontal plane for the head and front body-segments. To assess the sensitivity of the model to this parameter for the head and front body-segments, we implemented different modeling approaches, but the results were all the same. Consequently, for the head and front body-segments, frontal plane mobility needs appear to be accomplished by the combined movement in the sagittal and transverse planes. Alternatively, the task of walking at a self-selected speed the length of the walkway may not lend itself to mobility needs in the frontal plane for the head and front body-segments. The rear body-segment on the other hand, demonstrated a large amount of mobility in the frontal plane which was similar for both genotypes. That mobility is associated with the elevation and depression of each side during every walking cycle. It can be speculated, therefore, that frontal plane mobility of the rear-body may be related to the shock absorbing and propulsive capabilities of that side with every step and, therefore, it may be a reflection of the movement capabilities of each rear body-segment extremity function and walking speed. While both mice types performed similarly at their self-selected speed to meet the needs of their walking task, i.e., to walk the length of the walkway, it would be interesting to observe how this parameter may be affected by pathology and more advanced aging and/or PD-like pathology. While our current study

cannot provide answers to these questions, our model provides the opportunity to study these changes at a body-segment-specific level.

5. Conclusions

In conclusion, our manuscript presents a model which clearly provides the capability of quantifying and studying the distinct motion patterns of each body-segment of the rodent in a manner that angular displacement data are not sequence dependent, unlike when they are derived directly from rotation matrices. However, much like when human motion is considered, it may be of greater interest in the future to propose a model, founded on our current approach, which can describe the relative motion between the body segments of the rodent. We aspire that this will be the focus of our future efforts.

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HIGHLIGHTS

- We have constructed and fully presented a three-dimensional rodent kinematic model.
- The mouse consists of three segments, the rear body, the anterior body and the head.
- The unique description of each segment in space does not require long transformation matrices.
- The rotations are not sequence-dependent.
- The results are translatable to patients with Parkinsonism, demonstrating the models' translational efficacy.

Fig. 1.

This is the two-step model implemented. First the target model is shown with all the physical markers placed on the body-segments of the rodent. The picture on the right demonstrates the combined target model and kinematic model. The model shows the three body segments of the rodent (Rear body (C), Front body (B), Head (A)). The local body-segment coordinate systems are also shown (unit vectors $\hat{i}_1$, $\hat{i}_1$ and $\hat{i}_{1A}$ pointing in the anterior direction of the global reference system and of the body-segment system, $\hat{i}_2$, $\hat{i}_2$ and $\hat{i}_{2A}$ pointing in the medial–lateral direction of the global reference system and of the body-segment system, and $\hat{i}_3$, $\hat{i}_3$ and $\hat{i}_{3A}$ pointing in the vertical direction of the global reference system and of the body-segment system).

Fig. 2.

Rear body-segment motion in the sagittal plane (A), the frontal plane (B) and the transverse plane (C). Blue solid lines represent *Gdnf*^{+/-} mice, and red dashed lines WT mice. Positive rotation is extension in the sagittal plane, right side depression in the frontal plane, and right side forward rotation in the transverse plane. Note differences in posterior body movement between the two mouse strains, possibly suggesting a lack of flexibility in movement in *Gdnf*^{+/-} genotype compared to the age-matched WT strain. (For interpretation of the

references to color in this figure legend, the reader is referred to the web version of the article.)

Fig. 3.

Front body-segment motion in the sagittal plane (A), the frontal plane (B) and the transverse plane (C). Blue solid lines represent *Gdnf*^{+/-} mice, and red dashed lines WT mice. Positive rotation is extension in the sagittal plane, right side depression in the frontal plane, and right side forward rotation in the transverse plane. There are differences in movement between the two genotypes, especially in the sagittal and transverse planes. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Fig. 4.

Head body-segment motion in the sagittal plane (A), the frontal plane (B) and the transverse plane (C). Blue solid lines represent *Gdnf*^{+/-} mice, and red dashed lines WT mice. Positive rotation is extension in the sagittal plane, right side depression in the frontal plane, and right side forward rotation in the transverse plane. There were pronounced differences between the two genotypes, especially in the sagittal and the frontal plane movement. The data demonstrated in this Figure may suggest difficulty in head movement of the *Gdnf*^{+/-}

genotype. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

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Fig. 5.

Total body linear velocity of the two genotypes. Blue solid line represents *Gdnf*^{+/-} mice, and red dashed line WT mice. Note that the velocity in *Gdnf*^{+/-} was noticeably reduced and, therefore, it required almost twice the amount of time to reach the end of the walkway. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Table 1

Linear velocity of the total body in the anterior-posterior direction and range of motion of each body-segment of the rodents (*Gdnf*^{+/−}-type and WT-type) in three dimensional space based on the Euler angles: Pitch defining motion in the sagittal plane; Yaw defining motion in the frontal plane; Roll defining motion in the transverse plane.

Body Segment	Plane Motion	<i>Gdnf</i> ^{+/−} -type (°)	WT-type (°)
Head	Sagittal/Pitch		
	Max Flexion (−)/Max Extension (+)	2.13/24.85	20.66/72.65
	Range	22.72	51.99
	Frontal/Yaw		
	Max Depression Right (+)/Left (−)	−0.05/0.44	−0.62/0.28
	Range	0.49	0.90
	Transverse/Roll		
	Max Tilt Right (−)/Left(+)	−30.73/43.87	−30.64/32.46
	Range	74.6	63.1
	Sagittal/Pitch		
	Max Flexion (−)/Max Extension (+)	30.57/45.65	−0.96/39.41
	Range	15.08	40.37
	Frontal/Yaw		
	Max Depression Right (+)/Left (−)	−0.49/0.45	−0.49/0.35
	Range	0.94	0.84
	Transverse/Roll		
	Max Tilt Right (−)/Left(+)	−36.04/17.47	−27.78/45.18
	Range	53.51	72.96
Rear Body	Sagittal/Pitch		
	Max Flexion (−)/Max Extension (+)	19.24/39.64	10.58/39.93
	Range	20.4	29.35
	Frontal/Yaw		
	Max Depression Right (+)/Left (−)	−22.48/15.56	−21.66/11.76
	Range	38.04	33.42
	Transverse/Roll		
	Max Tilt Right (−)/Left(+)	−21.68/21.07	−23.03/35.20
	Range	42.75	58.23
Velocity maximum (m sec ^{−1})		0.13	0.26