Goal9 **Realization of a mentally healthy and dynamic society by increasing peace of mind and vitality by 2050.**

Realization of a society where people can live a forward-looking life in the face of adversity.

Here begins our new MIRAI

MOONSHOT RESEARCH & DEVELOPMENT PROGRAM

R&D item

2. Assistance and training for "Maemuki (Forward-looking mind)"

Progress until FY2023

1. Outline of the project

In this R&D item, we will develop training techniques that enable sustained improvement of the "Maemuki" component and techniques to assist in improving the "Maemuki" component (Fig. 1). We will also accumulate research findings on pharmacological and chemogenetic neurotransmitter manipulation in monkeys, and aim to establish "Maemuki" assist and training techniques that can be used in a manner that is tailored to the individual and situation.

2. Outcome so far

In FY2023, in addition to the construction of a technological foundation for "Maemuki" assistance and training, we accumulated necessary knowledge for establishing physical intervention methods for "Maemuki" mental manipulation and made preparations for applying the research findings on monkeys to humans. In addition, the research on molecular manipulation in monkeys provided us with essential research results for the full-scale launch of molecular manipulation research on "Maemuki" in the future.

● **Physical intervention target in gait for "Maemuki" Assist/Training**

In order to establish an effective intervention method for the body, it is essential to understand the "Maemuki" relationship between the body and the mind. We continuously recorded gait in daily life for 3 months to examine the characteristics of gait that are related to mental positivity. We found that several gait characteristics, including walking speed, were related to the "Maemuki" factor. We found an intervention candidate for improving "Maemuki" mind in a gait recording (Results of Dr. Takahiro Hirao's research group [QST]).

It is known that depressed patients show characteristic gait such as increased depressed posture, decreased vertical head movement, and decreased stride length, compared to non-depressed healthy participants. These gait characteristics may reflect positive and/or negative mental states, but it is unclear which gait is more closely related to mental states, because gait-related movements are chain-like. Dr. Natsuki Sado's research group (Tsukuba university) first focused on the depressed posture and examined the effects of intentional depressed posture on other gait traits. They found that an increase in depressed posture may lead to a decrease in gait. In this study, they also developed a method to evaluate the degree of depressed posture in detail by quantifying the degree of kyphosis of the thoracic spine.

● **Development of molecular manipulation techniques for monkeys**

The research group of Dr. Takashi Minamimoto (QST) has constructed a monkey cognitive task that incorporates elements of a cognitive task for humans created by Dr. Makiko Yamada (QST). Furthermore, they developed a paradigm for measuring and evaluating positive bias. With this development, we expect to apply the findings from their research with monkeys to humans.

Dr. Kenichi Inoue's group (Kyoto University) developed a monkey posture measurement system. By developing an artificial intelligence algorithm that estimates the 3D positions of feature points on a monkey's body from multi-camera videos using a constrained triangulation method, they have succeeded in estimating with high accuracy and quantitatively evaluating the posture of monkeys during free behavior in their cages.

Dr. Takashi Minamimoto and Dr. Kenichi Inoue have also developed a technique for manipulating neural activity in monkeys by implanting artificial receptors in the brain (Designer Receptor Exclusively Activated by Designer Drugs: DREADD). They have developed a vector for DREADD receptor that enables long-term and stable chemical genetic manipulation in primates and reported it in a paper (Kimura et al., Nature Communications, 2023).

3. Future plans

We are currently developing a "Maemuki" biofeedback training system for human participants. The system enables "Maemuki" mind training by comprehensively measuring biological signals during walking (gait, EEG, heart rate, respiration, and eye movement) and providing feedback on the degree of "Maemuki" of each individual based on his or her physical body. In the next year, we will first focus on the development of the EEG biofeedback system. We aim to complete the system by incorporating the results of this R&D, including the results of gait-related research.

In our research on monkeys, we plan to accumulate research findings, including findings that can be applied to humans, by verifying the relationship between "Maemuki" mind and physical posture using the cognitive tasks and movement measurement system which has developed.

JST **Japan Science and Technology Agency**