

## 1. Development and Measurement of “Maemuki (Forward-looking)” indices

### Progress until FY2024

#### 1. Outline of the project

In Research and Development Item 1, which aims to create and measure forward-looking indicators, we are working on optimizing forward-looking indicators and building models using various survey platforms. We conducted a large-scale online survey using a draft version of a subjective scale for forward-lookingness, performed item reduction and factor extraction for this subjective scale, and revised its items. In real-world measurements targeting top athletes, we administered the forward-looking scale and multidimensional physical measurements to athletes from different sports. Furthermore, we advanced the flow experience items of the forward-looking scale as a questionnaire scale that considers cultural differences, and an English version has been completed. Additionally, we have proceeded with the development of models to estimate forward-lookingness using laboratory data and open data.

#### 2. Outcome so far

Okay, here's the English translation of the provided Japanese text:

##### ● Mechanisms of Embodied “Forward-Lookingness”

We conducted large-scale surveys (cross-sectional and longitudinal) using the “Forward-Looking Scale” developed thus far. Furthermore, we created multiple cognitive tasks to evaluate the cognitive functions of forward-lookingness, and for some of these, we identified correlations with mood and memory, leading to a paper submission and conference presentation. By constructing a new machine learning method,

we succeeded in creating a model capable of estimating the degree of visual illusion and metacognition from positive illusion (individual data on the illusion of superiority), a key element of forward-lookingness (Matsuyoshi, Isato, Yamada, 2024). Moreover, by applying this method, we have built predictive models for well-being, well-going, and forward-lookingness in adversity, and are proceeding with further validation experiments. Additionally, as a result of examining the causal relationship between positive illusion (optimism bias) and mood from longitudinal large-scale survey data, we clarified that optimism bias influences mood (Isato, Aizawa, Miyamae, Yamada, 2024).

##### ● Real-World Sensing and Sports Performance Evaluation

We conducted surveys and interviews with a large number of athletes using a draft version of the forward-looking scale. Furthermore, in collaboration with athletes and sports organizations, we prepared measurement systems, developed the environment, and collected data during athletes' daily lives and actual competitions. Through blink analysis of formula car drivers, we succeeded in capturing changes in cognitive states (Nishizono, Saijo, Kashino, 2023). We also revealed that brain activity directly related to victory or defeat in esports appears immediately before a match (Minami et al., 2023). Additionally, we have conducted multidimensional measurements in the practical setting of a snowboarding competition and are proceeding with the analysis.

##### ● Circulation and Generalization of Forward-Lookingness through Flow Experience

In the creation of flow experience items for the forward-looking scale and the examination of cultural differences, we conducted interviews with students at the California Institute of Technology. We examined the validity of the items in a

Western cultural context and selected items deemed necessary for the forward-looking scale. Furthermore, we integrated these with a flow scale to complete a provisional English version of a combined Flow and Forward-Lookingness Scale.

Regarding experiments on the circulation and generalization of forward-lookingness, we created cognitive and behavioral tasks that induce flow experiences under various conditions and conducted preliminary studies. In addition to tabletop and screen-based games, we selected multiple flow experience tasks designed to generate solo/team flow, including full-body e-games and e-games co-developed with corporations. We then conducted multi-module biological measurements, including EEG, 3D motion capture, pupil/gaze tracking, and heart rate/respiration measurement.

#### 3. Future plans

Based on the achievements of fiscal year 2024, in fiscal year 2025 and beyond, we will continue multidimensional measurement experiments of psychology, brain, and body, as well as longitudinal measurements, to advance the optimization of the “Forward-Looking Scale” as a Well-going indicator. Based on the results of these surveys and experiments, we will prototype “Body2Positive,” a system for estimating subjective “forward-lookingness” from bodily information. We plan to further develop this into technologies capable of interpreting an individual's “forward-lookingness” and providing assistance and training.

## 2. Assistance and training for “Maemuki (Forward-looking mind)”

### Progress until FY2024

#### 1. Outline of the project

This research and development initiative aims to create training technologies that sustainably enhance “Maemuki” and assistive technologies that support such enhancement. The project also accumulates knowledge on pharmacological and chemogenetic manipulation of neurotransmitters in non-human primates, with the goal of establishing personalized and context-sensitive “Maemuki” assist and training technologies.

#### 2. Outcome so far

Techniques for inducing psychological “Maemuki” through gait and posture interventions have been validated, and real-time feedback systems using sensory stimuli have been developed. In addition, molecular manipulation technologies targeting non-human primates have been established, forming a foundation for long-term and selective control of neural activity.

#### ● Physical intervention target in gait for “Maemuki” assist and training

To investigate how changes in posture and movement during walking affect psychological “Maemuki”, Dr. Natsuki Sado’s research group (University of Tsukuba) conducted experiments involving posture interventions. Their work focused on depressive gait patterns such as slouched posture and short strides, and tested interventions like gaze guidance and posture correction to elicit more positive movement patterns. Through comparative analysis of ballet dancers and general female

participants, the group demonstrated that long-term posture training can influence specific body regions.

In parallel, Dr. Takahiro Hiraō’s research group (QST) developed a biofeedback system that utilizes sensory inputs such as optical flow and rhythmic sounds. This system analyzes multidimensional biosignals—including EEG, heart rate, respiration, gaze, and ground reaction force—in real time and provides feedback through auditory and visual stimuli. The group also used fMRI to examine how different types and presentations of visual stimuli affect motor sensation and brain activity, contributing to the development of sensory-based methods for inducing “Maemuki”.

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

In the domain of molecular manipulation, Dr. Takashi Minamoto’s research group (QST) applied chemogenetic techniques using DREADDs (Designer Receptors Exclusively Activated by Designer Drugs) to control neural activity. They used PET imaging to evaluate long-term expression stability and validated the effectiveness of neural manipulation. The group also developed AAV vectors targeting serotonin and dopamine systems, enabling selective and stable activation of specific brain regions. Furthermore, they created shortened DREADD constructs and vectors with selective expression in serotonin neurons to support precise neural circuit manipulation.

Complementing this work, Dr. Kenichi Inoue’s research group (Kyoto University) pursued structural optimization of viral vectors to balance expression efficiency and specificity. They successfully developed shortened DREADD constructs that

allow high-efficiency gene expression within size constraints. The group also established experimental systems to evaluate expression distribution and functional effects in the primate brain, and collaborated with Dr. Minamoto’s group to validate the effectiveness of these systems.

These achievements provide a strong biological and technological foundation for understanding the mechanisms of “Maemuki” and for advancing molecular-level research on psychiatric and neurological disorders. Future applications may include innovative therapeutic technologies based on neural manipulation.

#### 3. Future plans

Comprehensive measurement of biosignals during walking—including gait, EEG, heart rate, respiration, and gaze—is currently underway to estimate individual levels of “Maemuki” from physical data. By integrating insights from this research and previous findings on gait and mental state, the development of a biofeedback system capable of adjusting “Maemuki” is anticipated.

In primate studies, cognitive tasks and motion capture systems will be used to examine the relationship between “Maemuki” and body posture, with the aim of generating knowledge applicable to humans. For DREADD validation, in addition to PET (Positron Emission Tomography)-based expression confirmation, behavioral changes related to “Maemuki” and electrophysiological changes in brain activity will also be assessed.

### 3. Maemuki (Forward-looking) ELSI and social applications

#### Progress until FY2024

##### 1. Outline of the project

This R&D Item is responsible for the ELSI (Ethical, Legal, and Social Issues) and social application of “Maemuki (forward-looking)”. By accomplishing this R&D Item, we will evaluate Maemuki in various social situations and clarify the elements and degree of Maemuki leading to desirable mental states in populations with various attributes and situations (different life stages such as children, adults, and the elderly; different mental states such as palliative care patients and mania and depression). This will contribute to the project’s goal of developing positive estimation and assistive technologies.

The challenge in achieving this goal is that the definition of “Maemuki” is different depending on life stage and health status, and at the same time, it is difficult to conduct an objective evaluation method of Maemuki based on the same criteria because of differences in physical functions and body size. We are also working on the development of Maemuki evaluation and intervention methods that take ELSI into account, with the idea of assisting and training Maemuki in accordance with the individual’s situation and needs.

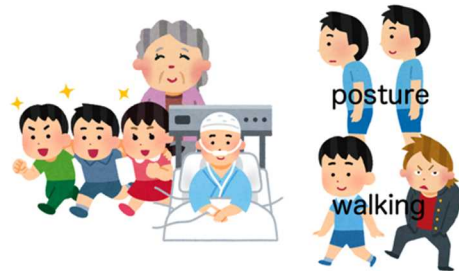


Fig.1 Evaluation of developmental stage, aging stage, and patient’s Maemuki based on posture.

##### 2. Outcome so far

###### ●Consideration of the significance and ethics of Maemuki

The research group of Dr. Shigeru Taguchi (Hokkaido University) has compiled a provisional reference guidebook on “positive functioning,” in which they examine and reflect on the concept of being “forward-looking” by considering the complex, multidimensional relationship between positive and negative life events from philosophical, psychological, and ethical perspectives.

###### ●The Relationship between Life Stages, Health Status, and Maemuki

The research group of Dr. Maiko Fujimori (National Cancer Center) conducted a study on creating a Maemuki scale for elderly and palliative care patients. The questionnaire survey results indicated no specific biases compared to the general adult population. However, it was suggested that elderly cancer patients scored significantly lower in aspects related to self-growth compared to younger cancer patients. Using natural language processing methods, content analysis identified gratitude related to interpersonal relationships and fulfilling obligations as contributing factors to Maemuki attitudes in cancer patients and the elderly. Additionally, a longitudinal study on palliative care patients suggested that patients who perceive their cancer as potentially curable have a higher one-year survival rate compared to those who perceive it as incurable. In terms of physical measurements related to Maemuki attitudes in the elderly and palliative care patients, data from gait analysis suggested that elderly cancer patients might be physically more fragile compared to younger cancer patients and healthy elderly individuals. Moreover, an examination of the relationship between body posture and emotions indicated that the physical function scores were lower under physical posture restrictions, and negative moods

were higher compared to the normal state.

The research group of Dr. Tetsuya Matsuda (Tamagawa University) and his research group conducted a data-driven analysis of lifestyle, Maemuki scale, and physical fitness among 1,365 university students through an online survey and physical fitness tests. Their analysis explored how lifestyle is related to physical, mental, and social well-being. The results suggested that lifestyle is indeed associated with these three aspects of well-being. Specifically, the findings indicate that individuals with regular physical activity tend to exhibit higher physical, mental, and social well-being levels. Additionally, the group analyzed gait and its relationship with positive functioning and lifestyle habits by capturing walking movements on video. They developed an AI-based automated gait analysis system and conducted gait motion analyses on approximately 1,000 participants. Using machine learning, they examined the associations between gait patterns and survey-based indicators, revealing a likely correlation between gait and indicators of positive functioning. Further detailed analyses are planned.

The research group of Dr. Hidehiko Takahashi (Institute of Science Tokyo) is collaborating with other PIs to investigate Maemuki attitudes in mental and neurological disorders. They are exploring methods for evaluating Maemuki attitudes and physical measurements. The study plans to enter a full-scale survey phase starting from the fourth year.

##### 3. Future plans

Studies targeting palliative care patients, older adults, and individuals in developmental stages are progressing, and patient-specific, life-stage-specific, and age-specific characteristics related to positive functioning are beginning to emerge. In parallel, the ELSI for “Maemuki” assistive training based on the needs of society will also be studied.

## 4. Overcoming adversity

### Progress until FY2024

#### 1. Outline of the project

This research and development item aims to identify the neural basis of perceived controllability in the face of adversity and to evaluate its predictive power for “Maemuki”, resilience, mental health, and well-being.

#### 2. Outcome so far

From this fiscal year, Dr. Michele Wessa and Dr. Klaus Lieb from the Leibniz Institute for Resilience Research (LIR) have joined the project, initiating detailed mechanistic studies on how perceived controllability under adverse conditions contributes to forward-mindedness and resilience.

##### ● Perceived controllability and its relation to depression

To investigate the role of perceived controllability in mental health and resilience, Dr. Michele Wessa’s research group conducted both an fMRI social stress study and a translational study. In the fMRI study (Kollmann et al., in prep), 120 healthy males were classified into high and low control groups based on perceived controllability, revealing that higher control was associated with less helplessness, fewer symptoms, stronger cortisol responses, and reduced insular activation. In a parallel study with 125 individuals showing subclinical depression, objective controllability reduced helplessness, stress, and negative cognitive bias, particularly buffering adverse effects in those with higher depressive symptoms. Additionally, the group performed re-analyses of cross-sectional data, identified latent control belief factors, and developed a predictive model of

resilience and well-being, which informs future prospective “Maemuki” studies.

##### ● Positive mental states and its relation to health and resilience

To investigate the relationship between positive mental states and resilience, Dr. Klaus Lieb’s research group and Dr. Michele Wessa’s research group developed a comprehensive rationale and timeline for a systematic review, which led to its prospective preregistration and the upload of the review protocol to the Open Science Framework. Literature searches were conducted across all relevant databases, and title/abstract screening has commenced. A first version of the study protocol was prepared for publication in BMJ Open (Max Supke et al.), in collaboration with PI Yamada (1-1) and PI Hamada (1-4). Training sessions with students were also conducted to ensure accurate and consistent screening procedures.

##### ● Perceived controllability and its underlying neural and physical correlates

To investigate the neural and physical correlates of perceived controllability, Dr. Michele Wessa’s research group engaged in a series of in-person and online meetings to discuss study designs, data collection methods, and preliminary results, in collaboration with PI Yamada (1-1) and PI Hirao (2-1). These collaborative efforts enabled the successful planning of prospective study.

##### ● Perceived controllability as a resilience mechanism in the general population and cancer survivors

Two workshops were successfully held — one in September and one in February — in Germany and Japan, respectively, to

discuss the study protocol and potential baseline measures for the longitudinal study, in collaboration with the research groups led by PIs Fujimori, Yamada, Hirao, and Hamada. Additionally, preparations for recruitment have been initiated, including the selection of LORA subjects and establishing contact with cancer units in Germany.

#### 3. Future plans

The project will continue to explore how perceived controllability and related positive mental states contribute to resilience, mental health, and well-being. Future activities will include data re-analyses, meta-analyses, and cross-cultural studies to deepen theoretical understanding and validate findings across populations. Collaborative pilot studies and the development of shared assessment tools are planned to support longitudinal research on stress and coping. Particular attention will be given to comparing general populations with individuals facing real-life adversity, aiming to clarify mechanisms and inform practical applications in both clinical and everyday contexts.