

2019 BSAC Report, RIKEN Center for Brain Science

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Introduction

The members of this advisory committee are honored to participate in the first BSAC review of the RIKEN Center for Brain Sciences. RIKEN established a world-wide reputation in neuroscience during the 20-year life of the Brain Science Institute. With its mission accomplished, BSI was phased out as scheduled in FY2017. After considerable thought, RIKEN decided to build upon its gains by establishing a new Center for Brain Sciences (CBS hereafter) devoted to the dual missions of understanding the human brain and mind, and to finding solutions to social challenges. CBS incorporates basic, applied, and translational research that will provide an essential foundation for understanding normal human brain function, for diagnosing and treating human neurological and psychiatric disorders, and for establishing a creative dialogue with the rapidly developing field of artificial intelligence. The BSAC endorses this wise decision by RIKEN!

Importantly, CBS is distinguished from BSI in its ultimate focus on the human brain, its dedication to creating tangible benefits for society, and its reorganization to align with the mid- to long- term plan and administrative practices of RIKEN.

We strongly endorse the selection of Dr. Yasushi Miyashita as the first director of RIKEN CBS. Miyashita has national and international stature as a neuroscientist of the very highest caliber, and he has chosen to devote this phase of his distinguished career to creating a novel and nourishing environment for neuroscience at RIKEN. Miyashita rightly recognizes the unique advantages of the outstanding interdisciplinary scientific environment at RIKEN. Convergence of concepts and techniques from multiple scientific disciplines is essential for the future of brain science; interdisciplinary effort on a large scale will be required for humans to make genuine progress in understanding our own brains! RIKEN is a potent intellectual environment, and Miyashita understands RIKEN's unique potential for incubating the next generation of cutting-edge brain science. Miyashita's presentation to the BSAC on the first morning of our meeting was a model of honest realism and visionary aspiration. Past and current problems were clearly articulated, but an optimistic vision provided substantial reason for enthusiasm about the future. We strongly endorse Miyashita's leadership of CBS. This was an inspired choice by RIKEN.

The past three years of transition from BSI to CBS have been difficult for many researchers and laboratories. The number of PIs was severely reduced from ~35 in BSI to ~27 currently in CBS, and the internal funding from RIKEN (i.e., Government Fund from RIKEN for BSI/CBS Operations; "internal budget", hereafter) was reduced as well. Making a successful transition to CBS has required an extraordinary amount of hard work and difficult decisions by many people, especially by Dr. Miyashita in his leadership role. Despite the difficulties, BSAC considers this transition to have been remarkably successful overall. It is a testimony to the patience, hard work and good will of the entire community.

The first critically important transition step was to establish a sound process for evaluating BSI Senior Team Leaders and making hiring decisions for CBS positions. BSAC feels that this process has been fair and reasonably transparent, incorporating several steps that are common to major universities and research institutes around the world (as described in the 2019 CBS Report): 1) evaluation by external letters from international leaders in neuroscience, 2) presentation by the candidate summarizing research accomplishments and future plans, 3) personal dialogue with CBS planning committee, 4) extended discussion within the planning committee, and 5) consensus hiring decision articulated by the director-elect. Also of critical importance was establishment of new CBS research management policies, including transparency in decision-making about capital equipment acquisitions and laboratory budgets and principles for sharing common resources.

Carrying out an international search and recruiting four new PIs in the past year is a milestone accomplishment for CBS. No new Team Leaders were hired in the last five years of BSI, which amounts to a death sentence for any scientific organization. Scientific vigor must be constantly renewed by an influx of talent and imagination in the Team Leader positions. The successful hires of the past year indicate a commitment of RIKEN to leadership in the brain sciences, the continued drawing power of the RIKEN environment for new Team Leaders, and the commitment of the current CBS researchers to carry out meticulous searches culminating in successful recruitments. BSAC applauds this milestone success.

Terms of Reference 1

TOR 1.1: Research.

The new Center for Brain Science is successfully conducting research that meets the highest international standards. This is demonstrated in the very high quality of the research outputs published in the best scientific journals, in the growing interest in CBS's research effort from other universities and outside organizations, and in the continued interest in collaborative relationships from corporations such as Toyota, Olympus and Kao.

The aim of CBS is to "*understand the human brain and mind, and through that to contribute to finding solutions to current social challenges*". This overarching aim is being achieved through an excellent organizational structure supporting four key research directions:

- Revealing the high-level cognitive functions of the human brain
- Identifying universal biological principles
- Collecting and applying big data, as befitting the technological age
- Tackling global challenges.

Striking discoveries have recently been reported by several CBS PIs conducting basic science. These include major steps forward in understanding the role of the hippocampus in memory published in two papers in *Science* in 2018. Examples of novel technology include non-invasive imaging technology that enables activity in specific brain areas to be visualized from outside the brain, and novel optogenetic technology that uses up-conversion of infra-red irradiation by nanoparticles to causally impact brain function. The latter discovery resulted in the first author, a postdoc at CBS, winning the prestigious Eppendorf & Science Prize for Neurobiology in 2019, a truly exceptional honor. Both innovations are world firsts, both also published in *Science* in 2018, and already attracting world-wide attention. The proportion of papers published by CBS investigators in high-profile journals is remarkable. Unique in the world, RIKEN has developed the first successful animal model of Alzheimer's Disease (AD) that avoids the artifactual use of transgenic over-expression of AD associated human genes, and this model is now being used in more 350 laboratories around the world. If a successful treatment for AD emerges from this worldwide effort, RIKEN will have a key place in the story. This is all the more likely from the wise decision to explore the use of marmoset monkeys in creating more valid models of brain diseases alongside research using mice.

TOR1.2 Contributions to Society

In terms of contributions to society, the work of CBS is strong, and emerges from one of the four major new research directions of CBS—the study of "*the universal biological principles of*

life". One such universal principle is care by parents of their offspring. At CBS, mouse models of infant care have already yielded understandings of relevance to human parental behavior, and now CBS scientists are well-poised to transition to the more complex (and human-like) parental behavior in the marmoset. These mouse and marmoset models will contribute to the understanding and treatment of human social behavior disorders in many ways, including interventions currently being tested or considered by international investigators in human social bonding failure such as medications (e.g. oxytocin), cognitive behavior therapy, or cell phone apps for in situ parental assistance. Interventions to build resilience of the parent-child bond against stress or neglect are globally important in today's world, where a range of stresses from political upheaval to addictive electronic messaging/gaming continually threatens fundamental human bonds. Furthermore, the CBS research output on language development has valuable implications for evidence-based childcare and early education, particularly in high-risk children. The ongoing prospective longitudinal studies of child development are expected to reveal globally applicable relationships between language and social development in children at multiple levels - behavioral, cognitive and physiological.

The enormous costs of neuropsychiatric disorders are well documented by the World Health Organization, with depression rising to the top in terms of cost worldwide. CBS is remarkably well-grounded in models of neuropsychiatric disorders. As a result, CBS is now having impressive international impact on treatment strategies for mood disorders (e.g. a new molecule patent for bipolar disorder), Alzheimer's Disease (the mouse and prospective marmoset models for drug testing) and betaine for schizophrenia, to name a few.

As is evident from these examples, CBS research is providing the world with basic knowledge and practical tools for combatting decline of basic social bonding, abnormal human development, and the devastating effects of neuropsychiatric disorders.

TOR1.3 Consistency with 7-year plan

The current aims of CBS are well aligned with the 7-year plan as outlined by Dr. Miyashita in his address on the first morning of the BSAC meeting. CBS's initial goal is to understand higher cognitive functions common to animals and humans, with the ultimate goal of addressing higher cognitive functions unique to humans. This research thrust will promote RIKEN's long term plan to create new research fields that address social needs and other national priorities.

An essential (and difficult) step toward reaching this ultimate goal was to evaluate the accomplishments and status of BSI and arrange a thoughtful, transformative transition to the new CBS. Before starting CBS, the Planning Committee evaluated BSI Senior Team Leaders according to strict international scientific standards as well as alignment of their research programs with CBS future goals. The Committee decided to recruit 17 of 24 BSI Senior Team Leaders to CBS while closing out laboratories of 7 others. The Committee also transitioned 10 of 11 BSI Team Leaders to CBS with specific plans to evaluate each Team Leader within the next few years according to the same international standards and program alignment that applied to BSI Senior Team Leaders. This major reorganization of existing labs, and the recent recruitment of 4 new PIs, are well aligned with the 7-year plan. The new PI recruitment has enabled four talented investigators to be appointed, of whom one will lead efforts to take human brain imaging into a new era of causal intervention, and another seeking to transform discoveries in model systems into potential treatments in psychiatry. A new Brain Medical Science Collaboration Division with the University of Tokyo will accelerate the critical task of translating fundamental discoveries to clinical application. As indicated in the

Introduction, recruitment of these new PIs to CBS is a major advance since no new PIs have been recruited to RIKEN neuroscience community since 2013.

Because human neuroscience figures prominently in the 7-year plan, it is essential for CBS to deploy state-of-the-art instruments for making measurements on the human brain. For example, the international standing of CBS will be enhanced through acquisition and expert operation of a 7-Tesla MRI scanner for noninvasive imaging of the human brain. In general, science advances across the board in tandem with advances in technology that permit new ways of approaching fundamental problems. Thus state-of-the-art equipment will also be needed in the Research Resources Division over the long run. Taken together, the activities and strategies CBS are on the right track for pursuing the 7-year plan.

Terms of Reference 2

Leadership

The SWOT analysis presented by Director Miyashita is well thought out and generally accurate, focusing on the major management issues that pose challenges to the future of CBS.

The BSAC was impressed by Dr. Miyashita's scientific stature, which ensures the respect of CBS scientists and RIKEN central leadership. The BSAC was also impressed with Miyashita's commitment to, and success in fulfilling, this challenging leadership position during the past two years. He has minimized the negative impact on scientific progress of closing BSI, and has maximized the opportunity to establish new scientific priorities with the opening of CBS. As summarized in the Introduction, Miyashita's management of the CBS appointment process has been exemplary.

Budget

The substantial annual reductions in the internal budget allocated to BSI and CBS by RIKEN HQ over the past six years is a **major challenge to the continued scientific excellence of CBS**. Dr. Miyashita's allocation of resources to competitive internal grants is a creative approach to addressing this challenge, as is his allocation of funds to share instrumentation resources that can create economies of scale. His encouragement of investigator applications to external funding entities, both Japanese and international, is and will continue to be important in addressing the budgetary challenge. However, financial creativity by the director and PIs can only go so far. Sustained budget cuts eventually eat away at the bone and sinew of the research enterprise, not just fat. We note with relief that the CBS internal budget was increased by ~5% in the current fiscal year, and we recommend strongly that this trend continue. CBS deserves financial support from RIKEN HQ and the national government that is commensurate with its stature as an internationally leading neuroscience institute. At the local community level, we encourage the CBS leadership to strengthen lines of communication within CBS to ensure that all PIs and lab members have accurate information about the current CBS budget situation and about external funding sources to which they can and should apply. Even though CBS is currently the most successful of all RIKEN centers in obtaining external funding support, further improvement seems possible.

PI recruitment/retention

As indicated in the Introduction, new PI recruitments are essential for the continued scientific vitality of CBS. Following 6 years with no new neuroscience recruits at RIKEN, Dr. Miyashita and the CBS leadership team have successfully recruited 4 new PIs in the past year (including a Hakubi team PI) and an additional 3 full-time and 4 adjunct PIs under CBS Collaboration Center and Divisions. This documents the effectiveness of Dr. Miyashita and his team (Deputy Directors Goda, Kamiguchi and Kato) as leaders and documents the high scientific stature of RIKEN CBS despite the turmoil of the past three years.

However, despite this success, the resources from RIKEN CBS that can be provided to jump-start the careers of young investigators is no longer considered competitive internationally, for example when bench-marked with resources provided by major institutions in East Asia, North America and Europe.

Similarly, the current RIKEN salary cap means that CBS cannot provide sufficient compensation to senior investigators to ensure their retention, does not adequately reward exceptional scientific contributions, and may potentially affect future recruitments, especially of international investigators. We understand that the salaries of some tenured CBS PIs are currently frozen because they exceed the RIKEN salary cap, which is well below salaries at peer institutions. In effect, these investigators are being forced to accept a *reduction in real salary*, which will inevitably lead the best PIs to consider options elsewhere. Similarly, the age limit for RIKEN tenure assurances (60, though can be extended to 65 after evaluation) is very unattractive compared to peer institutions, and thus incentivizes top PIs to look elsewhere.

Scientific environment

An essential component of any world-class scientific environment is constant exchange and critical evaluation of current scientific projects and ideas, both within the local institution and between institutions nationally and internationally. Major research universities and institutes promote community intellectual vigor through regular seminar series, journal clubs, research-in-progress lunches, retreats, and other similar mechanisms. Given the enormous challenges of the transition period, it is understandable that these community events have not been a top CBS priority list during the past two years, but it is time to bring them back to the forefront. Our interviews with PIs, postdocs and graduate students all indicate that community events are highly desired at all levels. Thus BSAC strongly endorses Dr. Miyashita's plan to re-establish a CBS-wide seminar series and additional scientific and social events as well. International speakers, in particular, can serve as ambassadors in their home countries to report on the scientific strength of an institution they have visited. The seminar series and additional scientific and social events will foster interaction between the CBS community and prominent outside researchers, and will promote dialogue and collaboration between CBS scientists at all levels. Importantly, these events will help postdocs and PhD students form supportive networks that enhance scientific growth and future career opportunities. Similarly, Dr. Miyashita's recent establishment of an annual CBS retreat is greatly appreciated by all CBS scientists.

Diversity in the Workforce

The imbalance in gender among CBS scientists was correctly identified as a weakness in Director Miyashita's SWOT report. Only ~18% of CBS PIs and ~25% of CBS researchers are female. Although this compares favorably to gender representation in life science divisions at Japanese universities, this is well behind current standards at international peer institutions, which themselves need to improve. RIKEN in general and CBS in particular can and should do more to recruit female

colleagues and create an environment that welcomes women and optimizes their research and career advancement opportunities, including equal financial, space and equipment resources for their research programs. This applies at all levels—graduate students and postdocs in addition to faculty. BSAC suggests specific mechanisms for working toward this goal in our recommendations.

Postdoctoral and graduate student training

BSAC agrees with Dr. Miyashita and the CBS PIs that talented postdocs/research associates are critical to the continued success of CBS, and with strongly support Dr. Miyashita's prioritization of "Fostering Young Scientists" as one of the three key missions of CBS. From our discussions with postdocs and graduate students, it is clear that both groups recognize and are proud of their privileged situation at CBS. RIKEN CBS's international scientific environment, quality of research, and superb facilities are key factors that make CBS attractive for postdoctoral and graduate training.

However, BSAC shares Dr. Miyashita's concerns regarding the slow career development of postdoctoral fellows, and as a consequence, the aging of postdoctoral cohort (roughly a third are now over the age of 42). The reasons for this are complex, and certainly include a scarcity of job openings for academic scientists at Japanese universities. Nevertheless, the problem can be positively addressed through more active career mentoring for postdocs. For example, BSAC strongly commends the recent creation of a career development program for postdocs. This is an excellent step forward.

Individual PI-postdoc relationships can be difficult to assess, but some information is available. From our discussions with postdocs, and from the anonymous feedback to the survey that we received, it is clear that many postdocs are pleased with their mentoring relationships, but others are frustrated by a lack of quality mentoring. One core problem seems to be that some PIs regard postdocs mostly as a source of laboratory labor rather than as valued junior colleagues who need quality mentoring and training to develop their careers and become thriving scientific leaders. From the individual laboratory reports in the large CBS Report, it appears that there are significant disparities in how successful different labs are in placing their alumni in high quality research positions. Regular, proactive mentoring could move postdocs through CBS in a more timely manner and reduce the overall age of the postdoctoral cohort. We suggest specific mechanisms in our recommendation below, several of which are already anticipated in Dr. Miyashita's presentation on the first day of the BSAC meeting.

As indicated above, the graduate students who attended our discussion were generally very positive about their experience at RIKEN. BSAC was surprised by how few complaints there were! One frustration that was mentioned by several students was difficulty in interacting with their home institutions. The students have a hard time getting the attention of administrators and faculty at their home institutions, and book-keeping items require much more time and investment from RIKEN students than from their peers who are physically present at the home university. (This problem is less pronounced for students whose RIKEN PIs are also adjunct faculty at their home institutions.) BSAC encourages CBS to support students in coordinating their interactions with home universities. Students liked the idea of a RIKEN-wide graduate student association that holds regular scientific and social events, but they also liked the idea of joining the activities of the new CBS postdoctoral association. Students were very positive about their relationships with the postdocs in their individual laboratories. They feel supported by the postdocs and seem to respect them highly.

Shared equipment facilities

The BSAC was impressed by the quality of the CBS core facilities, but also appreciated that several services are not widely used by CBS investigators. The comparatively small size of CBS creates a challenge for the CBS cores to meet all technological demands through acquisition of the most modern equipment and support by well trained personnel. The move by CBS to open the core facilities to laboratories in other RIKEN life sciences centers is both wise and collegial. Costs can be supported with a larger base of users without affecting the quality of the products delivered. However, given financial constraints, the management might consider reducing the personnel somewhat.

BSAC supports current collaborations with industries and is enthusiastic about continued efforts to identify potential areas for CBS-industrial collaboration. CBS is especially well positioned to create collaborations in imaging technology development. This can provide useful supplementation to the CBS budget and expand opportunities for CBS investigators.

Terms of Reference 3: Internationalization and Collaboration

Internationalization

CBS (and BSI) has made significant efforts to recruit international PIs, postdoctoral fellows and graduate students. The resulting numbers document the success of this effort: 19% of CBS PIs and 36% of CBS research scientists are from abroad, making CBS the most internationally integrated of all RIKEN bioscience-oriented centers according to Director Miyashita's report. As summarized in Dr. Miyashita's presentation on the first morning of the BSAC meeting, CBS has established joint programs with Harvard, UCSF and MIT, and has created ties with several other leading universities around the world. These accomplishments are clearly substantial, and we salute them.

Nevertheless, efforts toward internationalization of the CBS workforce must continue to be vigorously pursued in the future to ensure the excellence and international prominence of RIKEN and CBS research programs. Under BSI, a PhD level scientist was assigned to promote RIKEN neuroscience widely by giving talks and visiting with faculty, postdocs and students at many international universities and research institutes. BSAC members from outside Japan can testify that these efforts greatly helped in putting BSI on the map in foreign countries. Another mechanism that has been useful in recruiting international trainees and even PIs to BSI and CBS is the annual summer course. BSAC notes that, for budgetary reasons, the duration of the summer course (lecture course) has been reduced from 2 weeks in the past to one week after 2012 (internship course continues without change). BSAC wonders whether the reduction should be reconsidered. BSAC also suggests that each lab webpage contain an alumni site. Seeing the names of alumni, time spent in the lab, and present prestigious positions can help recruit high quality postdoctoral candidates from foreign countries and from inside Japan as well.

A significant challenge to internationalization is the lack of foreign-born PIs in leadership positions at RIKEN HQ and CBS. BSAC understands that there are barriers to this goal (language being foremost), but if RIKEN is truly serious about internationalization, international scientists cannot be relegated to second-class status in the management hierarchy.

Collaboration

RIKEN has established a program to enhance its function as the core organization for research partnerships in Japan, called the "Science and Technology Hub". CBS's research activities in

support of this important RIKEN function have been outstanding, as illustrated by the detailed diagram of interlocking CBS collaborations in the CBS Report (Figure 6, page 25). The figure shows 16 different collaborations grouped into 4 main clusters: the Core Institute for Brain/MINDS, the Brain Medical Science Collaboration Division, Integrative Computational Brain Science Collaboration Division, and Centers for Collaboration with Industry.

Collaborative activities: Brain/MINDS

Brain/MINDS is a 10-year (FY2014-2023) Japanese flagship brain project funded by AMED (Japan Agency for Medical Research and Development). It is an internationally recognized initiative for exploration and discovery of knowledge-based strategies for the eradication of major brain disorders, hosted at RIKEN CBS. A central focus is development of novel neurotechnologies, particularly targeting the common marmoset as a nonhuman primate model of nervous system diseases and disorders. At its 5 year interim evaluation, Brain/MINDS was highly rated for achievements on structural brain mapping and technology development. The evaluating team made several important recommendations, which CBS implemented with considerable reorganization of the Brain/MINDS research groups, including recruitment of several laboratories outside RIKEN as adjunct Brain/MINDS research sites. The net result was to intensify and diversify the collaborative Brain/MINDS network.

In 2018, a new AMED Project (Brain/MINDS Beyond) was launched, centered on the National Institute for Physiological Sciences (NIPS), that aims to develop and integrate brain imaging technologies for healthy and diseased subjects and across species. CBS expects to strengthen collaborations with this project as well. Similarly, the International Brain Initiative (IBI) has been launch as an effort to intensify collaborations between several national brain initiatives including the USA BRAIN Initiative, the Human Brain Project in the EU, Brain/MINDS in Japan and several other countries as well. RIKEN CBS is expected to assume a role as one of the core IBI contributors.

Development of the marmoset as a genetic model for neurological and psychiatric disease has generated tremendous interest around the world, and RIKEN CBS will clearly have an important, world-wide leadership role in development of this new primate model during the next decade. This scientific development will provide CBS scientists with great access to the rapidly developing knowledge base, infrastructure and transgenic lines for marmoset studies. Marmosets are already playing an important role in the research on neurodegenerative disease and neural mechanisms of social bonding between parents and offspring. BSAC believes it is important that these and other CBS laboratories establish collaborative arrangements to take advantage of Brain/MINDS infrastructure and transgenic lines. The success of Brain/MINDS should be a big win for multiple research programs at CBS.

Collaborative activities: Brain Medical Sciences

The Brain Medical Science Division, led by Dr. Shigeo Okabe, is developing platforms for facilitating collaboration between RIKEN CBS and medically oriented universities and research institutes in Japan. In the past year the Division began a strong collaborative program with the University of Tokyo Medical School by establishing two laboratories on brain dynamics using a joint appointment mechanism. In addition, CBS plans to create collaborative arrangements with hospitals at NCNP and Juntendo University.

Looking to the future, there are comparatively few scientists at CBS who actively collect human subjects data for their research. Recruiting more clinician-scientists as Team Leaders would align well with CBS's 7-year plan to increase research that is directly applicable to human disorders and societal problems.

Also for the future, CBS should monitor important developments from the field of large scale human genetic studies (e.g. the Psychiatric Genetics Consortium) that are identifying many genes conferring risk for neuropsychiatric disorders. Each of these gene markers can be immediately applied to research in animal models such as humanized transgenic mice. Clearly CBS, with its best-in-class pre-clinical models, is ideally situated to capitalize on the surging flow of risk gene information. Furthermore, these hundreds to thousands of small-risk genes can be combined together into a single gene panel test, a 'Polygenic Risk Score (PRS)' that can score new sets of patients regarding their risk for the disorder in question, e.g. bipolar disorder, depression, schizophrenia, Alzheimer's, and so on. Thus high-risk persons can be readily identified and recruited into studies of biomarkers (biochemical, neuroimaging) and into clinical trials of new treatment strategies.

The Big Data produced globally regarding genetics of neuropsychiatric disorders is available to authorized users, and CBS could advantageously be a hub for movement of these risk gene data into preclinical models within RIKEN, and outward to partners doing clinical trials and other applied interventions.

AI and machine learning hold great promise for improving medical science over the next decade. These technologies provide tools for analyzing large datasets, which can help doctors make better diagnoses and improve medical care. Equally important will be the impact of machine learning on advancing our understanding of complex medical problems, including psychiatric and neurological disorders.

CBS could serve as hub in organizing efforts to deal with big medical data generated by its medical partners. AIP already has several groups working on these problems, including teams on Machine Intelligence for Medical Engineering, Data-Driven Biomedical Science and Computational Brain Dynamics (<http://www.riken.jp/en/research/labs/aip/>). A partnership between CBS and AIP directed toward genetic disease could have great synergistic value to both Centers and to the greater medical community in Japan.

Collaborative activities: Computational Neuroscience

In the last several years during the BSI era, many theoretical and computational neuroscientists were lost: Cichocki, Diesmann and Grün returned to Europe, and Amari, an icon in theoretical neuroscience, retired. Fukai was recruited to CBS but decided to take a tenured Professor position at OIST. Only Nakahara and Toyozumi remain at CBS, but given the growing demand of computational approaches in neuroscience, recruitment of excellent theoretical and computational neuroscientists is urgently needed.

Recruiting top computational researchers is highly competitive in both industry and the academia, which will make it difficult to hire computational PIs in the next round of CBS recruiting. The planned workshop on "Theory towards Brains, Machines and Minds" in Tokyo later this year could help draw the attention of theoretical/computational researchers to opportunities at CBS. Further activities, such as recruiting at major computational conferences, should be considered.

RIKEN AIP is facing similar difficulties in building up their faculty. Japanese trainees in the computational sciences receive lucrative job offers in industry after receiving their master's degree. A partnership between CBS and AIP could help both Centers through joint recruiting of computational faculty and postdocs. Masashi Sugiyama, the director of AIP, is a distinguished leader in machine learning and is interested in joint efforts with CBS, especially in the development of neuro-inspired AI. AIP will open an office at the Wako campus shortly, which could serve as a point of contact with CBS. Synergy with AIP could also benefit CBS when it is reviewed by RIKEN in six years.

The marmoset project in Brain/MINDS produces big data from anatomical studies and recordings of neural activity. These require not only massive data storage and processing infrastructure but also expertise in statistical analysis and modeling. No theoreticians from BSI except those in Yamaguchi lab were interested in helping with the analysis of marmoset data, and Brain/MINDS therefore relied on external researchers from Kyoto University and OIST. Recently, two young data scientists were hired as Unit Leaders under Brain/MINDS and one theoretician as a joint appointment Team Leader; tight collaboration between these new recruits and the rest of the CBS community would be a smart move. Theoretical and computational researchers at CBS can serve as a bridge between Brain/MINDS and the rest of CBS.

The data-intensive nature of modern science, including neuroscience, will inevitably create an expanding need for computational infrastructure and expert data management pipelines in addition to computationally oriented PIs. RIKEN, like many universities and research institutes worldwide, should invest in joint data management and computational infrastructure that can be shared by RIKEN labs.

Collaborative activities: Industry

CBS continues to have productive collaborations with industry through ongoing programs with Olympus, Toyota and Kao. The Olympus collaboration focuses on development application of new imaging technologies. This CBS-Olympus collaborative center (BOCC) is ably supervised by Dr. Miyawaki, a wonderfully creative neuroscientist. State-of-the-art instruments are conveniently located in the CBS central building and are open to all RIKEN researchers, a generous arrangement that we applaud. Importantly, CBS and Olympus scientists continue to collaborate on new technology development such as irradiance meters, flexible handling microscope stages, software for multicolor imaging (freely available online), and next-generation detectors for 2-photon microscopes. Any university or research institute would be fortunate to have an innovative facility like this on their campus.

The CBS-Toyota Collaboration Center (BTCC), directed by Dr. Yasuo Kuniyoshi, seeks to apply technological innovation to understanding and improving human cognition in normal and disease conditions. Begun in 2007, BTCC first concentrated on remote driving, robotics, and technological assistance for paralysis and stroke victims such as the BMI-controlled wheelchair. Addition projects have included analysis of brain dynamics, specifically EEG-measured brain rhythms and mechanisms of brain adaptation to environmental change. Stage IV of the collaboration was initiated in 2018 with a new focus on human decision-making at the individual and collective levels, incorporating principles and insights from neuroeconomics, behavioral economics, psychology and cognitive science. The overall goal, which aligned well with the RIKEN-CBS mid- to long-term plan, is to advance scientific understanding of human cognition and to create sustainable designs for effective social systems. The CBS-Toyota appears to be thriving with meaningful input from both sides on project planning and execution.

The CBS-Kao collaboration is focused on the interface between perception and emotion. It is directed by Dr. Hitoshi Okamoto of CBS and involves several other CBS laboratories including those of Dr. Yoshihara, Dr. Kazama, and Dr. Murayama. The Kao corporation designs and markets consumer products oriented toward the five senses, and wishes to understand how humans make value judgments and establish preferences. This emotional aspect of perception, captured by the Japanese word, *kansei*, is also of substantial interest to neuroscientists who seek to understand how sensory signals in the brain interact with affective signals to influence perceptual decisions. This line of research is also well aligned with the CBS mid- to long-term plan focused on human cognition.

Collaborative activities: Startups

RIKEN and CBS want to return value to society. One way this could be done is through innovative startup companies spun off from scientific advances. A good example from BSI is HACOSCO (<https://hacosco.com>), started by Naotaka Fujii who gained expertise in virtual reality technologies for his monkey experiments. CBS faculty should be encouraged to consider a broad range of possible patents and applications of their research results and methods, not limited to pharmaco-medical applications. The most promising new ideas could be incubated through the new venture wing of CBS. Transparency of the CBS policy on startups is essential for achieving the goal of having an impact on society.

Terms of Reference 4

As summarized elsewhere in this report (e.g. TOR 1), the overall performance of CBS PIs is exemplary. The number of BSI/CBS PIs declined by almost 50% between 2009 and 2018, yet the number of high profile publications per lab doubled during the same period, which is remarkable! Increasing high quality scientific output during a difficult time of reductions and transition testifies eloquently to the quality and determination of the PIs, and to the care and thoughtfulness that has gone into CBS hiring decisions. The scientific research of the CBS PIs unquestionably meets international standards, as is evident from our own conversations with Center PIs and through examination of bibliometric data. In addition, the research activity of current PIs and the new PI hires made in 2019 is well aligned with the 7-year plan, as summarized in TOR 1 of this report. Effective laboratory management is becoming an increasingly important issue worldwide. Many CBS PIs are excellent at laboratory management and mentoring of junior scientists, while some are still learning. Director Miyashita has articulated goals for strengthening the mentoring of postdocs and graduate students, which BSAC strongly endorses. Overall, RIKEN should be extremely pleased with CBS's performance record, as is this BSAC.

BSAC 2019 Recommendations

Recommendation 1: To support the human cognition component of the 7-year plan, BSAC recommends purchase of a 7T MRI scanner, and recommends that appropriate support personnel are recruited (or assigned) to run the instrument and establish data acquisition protocols.

Recommendation 2: BSAC strongly recommends continued yearly increases in the CBS internal budget allocated by RIKEN HQ to support and expand CBS scientific activities.

Recommendation 3: To fulfill the 7-year plan for CBS, a critical mass of investigators is needed in high priority areas identified by Director Miyashita. BSAC recommends hiring at least 7 new PIs (in addition to the 2019 recruits) as projected by Dr. Miyashita. RIKEN HQ should consider reform of its salary and age caps to incentivize excellence and facilitate PI retention.

Recommendation 4: BSAC recommends proactive steps to promote intellectual exchange and community building among CBS researchers. A regular seminar series should feature distinguished external and internal speakers with opportunities for trainees as well as PIs to interact with the speakers. Regular research-in-progress lunches and journal clubs should also be considered.

Recommendation 5: The BSAC recommends continued efforts to rectify gender imbalance through a focus on recruitment of both junior and senior women investigators. Successfully recruited women faculty must be well supported in realizing their scientific potential. Useful mechanisms that might be considered include 1) establishing a “women in science” association at RIKEN CBS to support women at all career stages, 2) providing a senior faculty mentor or mentorship committee for all new PI recruits, including at least one senior woman for female PI recruits, 3) increasing the number of women speakers in a re-invigorated seminar series with the aspirational goal very close to an equal gender balance, 4) including women on all hiring committees, 5) education of PIs and staff on implicit gender bias issues.

Recommendation 6: BSAC recommends creation of mentorship committees for postdocs, and if possible for graduate students as well. For example, 3-4 committees could be created that together cover the relevant subfields of neuroscience. Each committee could include CBS PIs with expertise in the subfield, and perhaps faculty from nearby universities if appropriate. Each committee would advise multiple postdocs in its subfield. Committees should meet annually and provide candid feedback to individual postdocs about project and career progress. For postdocs with academic aspirations, committees should help identify opportunities for gaining teaching experience.

Recommendation 7: The BSAC commends CBS’s leading role in integrating scientists with international experience. BSAC recommends continued recruitment of international scientists at all levels and integration of international PIs into CBS and RIKEN management.

Recommendation 8: BSAC fully supports the decision to explore the potential of a non-human primate, genetic model (the marmoset) to investigate brain disease, but recommend that RIKEN explicitly recognize that the timescale for exciting findings may be longer than in other fields.

Recommendation 9: To facilitate societally important medical research collaborations, CBS can consider hiring PIs with dual clinical and research expertise.

Recommendation 10: CBS should consider hiring PIs with computational expertise—perhaps in collaboration with AIP—in light of the increasingly important role of computation in all areas of neuroscience.

