Realization of a society where child abuse and suicide are zero

### R&D item

# 1. Brain AMPA receptor data and epigenome data for abuse and suicidality

## Progress to date

#### 1. Outline of the project

By using the positron emission tomography (PET) tracer alpha-amino-3-hydroxy-5-methyl-4technoloav for isoxazole propionic acid (AMPA) receptors recognition for human living brain, which we developed for the first time worldwide (Miyazaki et al., Nature Medicine 2020), we aim to perform AMPA-PET imaging on young adults who have experienced abuse in childhood and analyze the densities of AMPA receptors in their brains. We compare these with AMPA-PET data from sex/age-matched healthy controls (already constructed) and identify the brain regions where AMPA receptor levels differ in relation to histories of abuse and suicidal tendency. Through these efforts, we aim to clarify the brain mechanisms underlying the emotional instability that can lead to suicide from the biological effects of abuse history in childhood. We also aim to obtain

#### R&D Item 2: Brain AMPA receptor data and epigenome data for abuse and suicidality

	Twenties cohort			
	Abuse history	+	+	-
	Suicidality	+	-	-
The world's first AMPA receptor recognition for human brain related to abuse and suicidality • Amount of region-specific AMPA receptors • Association with DNA methylatic data on peripheral blood from same individuals				

comprehensive DNA methylation data for the same individuals and examine the relationship between AMPA-PET and epigenome data.

#### 2. Outcome so far

We have started to obtain AMPA-PET data and comprehensive DNA methylation data from the individuals after completing the ethical approval procedures. As the result of the interim analyses, we found that the densities of AMPA receptors are significantly increased throughout the whole brain in all three cases with histories of severe abuse and current suicidal tendency, compared to the healthy controls. Particularly, the increases in AMPA receptor densities were most prominent in the case individual with the highest score for adverse experience. The findings here



were completely different AMPA receptor changes from those we have ever seen in patients with other psychiatric and physical diseases in our AMPA-PET research. If similar changes are observed in other future cases of abuse history and suicidal tendency, we believe that we acquire new findings that the increase in AMPA receptors throughout the brain have relation with biological basis of the abuse and suicidal tendency of young people, independent of the effects of other psychiatric diseases and problems.

Here begins our new MIRAI

MOONSHOT

#### 3. Future plans

Even worldwide, this is the first study focusing the histories of abuse and suicidal tendency using AMPT-PET imaging, which may discover central nervous system changes specific to young people with the histories of abuse and suicidal tendency the first in the world. We keep to promote recruitment (the below) and aim to accumulate

more data (e.g. conducting multi-center research). We also perform correlation analysis with the epigenome data in the peripheral blood samples obtained from the same time and investigate the utility of the epigenome data as a peripheral biomarker of changes in brain AMPA receptors.



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