

# Brain aging in cynomolgus macaques and common marmosets explored by mapping the magnetic susceptibility and $R_2^*$

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## INTRODUCTION

- Brain aging involves a complex process of restructuring, including, but not limited to, volume loss, changes in white matter integrity, and iron accumulation.
- All these findings have likewise been observed in neurodegenerative diseases in humans.
- Non-human primates (NHP) are indispensable models in biomedical and preclinical translation research due to their similarities with humans.
- NHPs may be particularly suited as models of healthy aging in humans.
- Quantitative susceptibility mapping (QSM) and  $R_2^*$  maps are particularly sensitive to iron and myelin<sup>2,3</sup>. The different manner they respond to tissue changes may be used to disentangle processes evolving in parallel during aging.
- This study aims to assess changes in QSM and  $R_2^*$  values of gray and white matter regions with aging in healthy macaques and marmosets.**

## METHODS

- In this study, 13 clinically healthy female cynomolgus macaques (*Macaca fascicularis*), and 32 healthy marmosets (*Callithrix jacchus*) were included.

Macaque		Marmoset			
Age (yr.)	7 - 8	2	4 - 6	7 - 10	12 - 15
Animals	4	7	7	10	8

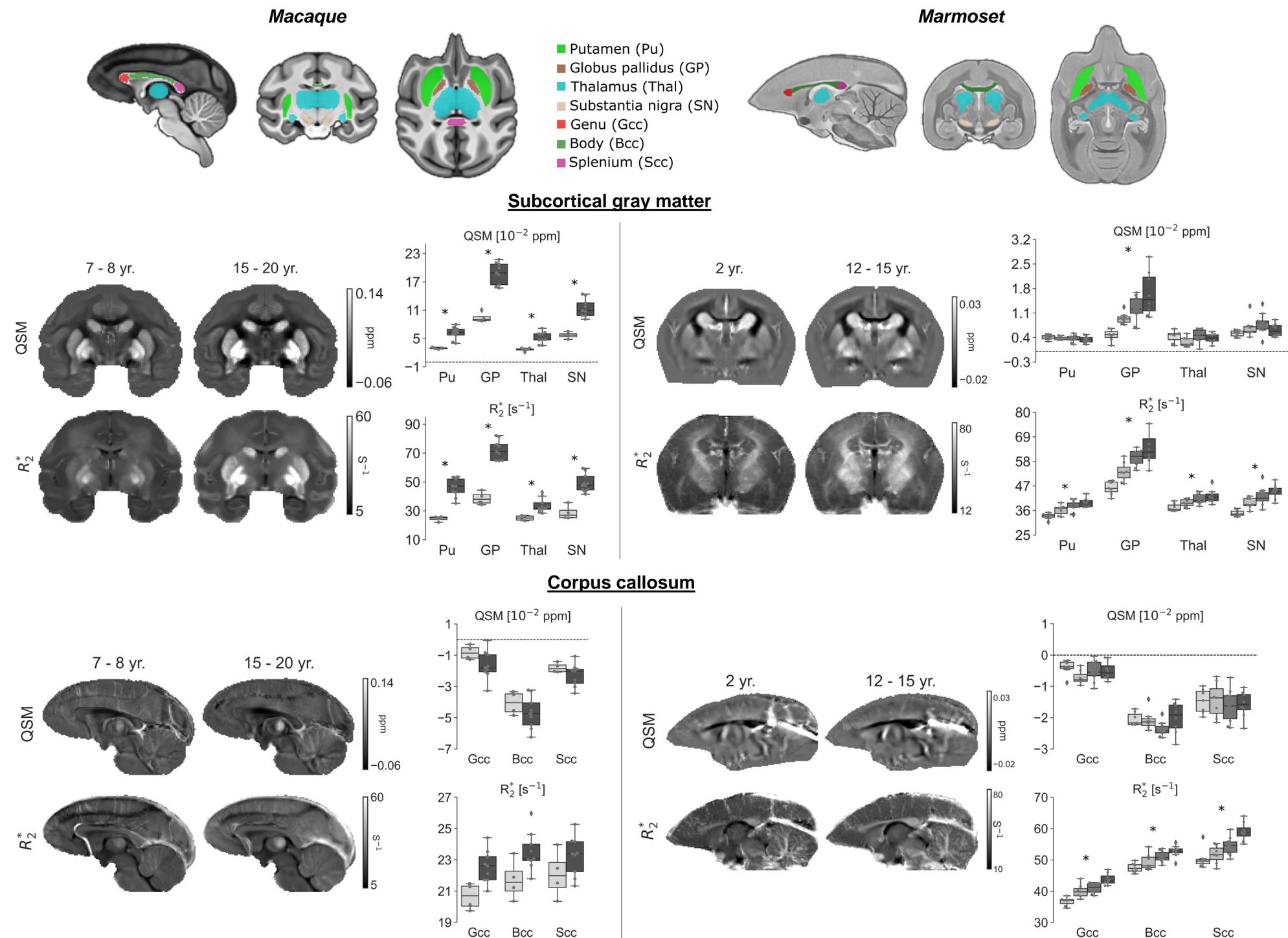
- A multi-echo gradient echo sequence (ME-GRE) was used to acquire phase and magnitude images.
- QSM reconstruction was carried using the multi scale dipole inversion approach<sup>2</sup>.
- The  $R_2^*$  maps were estimated by fitting the magnitude signal decay.
- The macaque and marmoset age-specific templates were constructed by aligning all species-specific QSM and  $R_2^*$  maps in the same space<sup>4</sup>.
- ROIs were propagated from the CHARM<sup>5</sup> and SARM<sup>6</sup> atlases (macaques) and the MBM atlas<sup>8</sup> (marmosets).

	Macaque	Marmoset
scanner	3 T Siemens MAGNETOM Prisma	9.4 T Bruker BioSpin
coil	single loop	single loop
sequence	3D ME-GRE	3D ME-GRE
resolution (mm)	0.31x0.31x0.31	0.21x0.21x0.21
repetition time (ms)	57	42
echo time (ms)	3.7/ 4.9/ 48	3/ 3/ 30
flip angle (deg)	20	25
acquisition time (min)	24	17.5

## References

- Betts, M.J., et al., 2016. Neuroimage 138; 2. AcostaAcosta-Cabrero J., et al., 2018. Neuroimage 183; 3. Langkammer, C., et al., 2012. Neuroimage 62; 4. Avants, B.B., et al., 2011. Neuroimage 54; 5. Jung, B., et al., 2021. Neuroimage 235; 6. Hartig, R., et al., 2021. Neuroimage 235; 7. Rohlfing, T., et al., 2012. Front. Neuroinform. 6; 8. Liu, C., et al., 2020. Nature Neuroscience 23.

## RESULTS



- The globus pallidus and other subcortical gray matter nuclei showed a significant increase in QSM and  $R_2^*$  values with age in both species, although to a different extent.
- QSM values of white matter structures, such as corpus callosum, followed a decreasing trend with age in macaques only.
- In contrast to QSM values, the  $R_2^*$  values increased in cortical, subcortical grey, and white matter structures.

## CONCLUSION

- QSM and  $R_2^*$  values in subcortical gray and white matter areas followed a similar trend as reported for humans with age (Betts, M.J. et al., 2016).
- Compared to macaques, marmosets showed only minor or no changes in magnetic susceptibility with increasing age. Whether this reflects different aging processes or may be related to technical issues (e.g., magnetic field strength) must be clarified in further studies.