Depressive symptoms and white matter structure in older adults with and without diabetes mellitus

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Introduction:

Aging is associated with a higher risk for developing type 2 diabetes mellitus (T2DM). Importantly, T2DM is often associated with major depressive disorder (MDD), and its comorbid occurence is linked to an increased risk of mortality [1]. Both diseases are linked to alterations of white matter (WM) structure, e.g. increases in WM hyperintensities or degeneration of WM tracts, such as the anterior cingulum [2]. Whether the reported WM changes in T2DM and MDD would be altered by comorbid occurrence, however, remains to be explored. Therefore, the current study investigated the relation between T2DM, depressive symptoms and WM structure (i.e. WM hyperintensities and structural connectivity (SC) of the anterior cingulate cortex (ACC)), in a large population-based cohort of older adults.

Methods:

From the initial group of 630 older adults (mean age 63.4 ± 12.1; 47% female; recruited from 1000BRAINS [3]), 568 subjects had a negative history of T2DM and represented the healthy control group (HC). The diabetes group (DG) comprised 62 subjects with diagnosed T2DM of which 37 exceeded an HbA1c cut-off value of 6.5%. Depressive symptoms were assessed via the Center for Epidemiologic Studies Depression Scale (CES-D) composed of 15 items, with higher values indicating a higher depressive symptomatology [4]. Localization and volume of WM hyperintensities were extracted from structural brain images (T1 and T2-weighted FLAIR carried out on a 3 Tesla MR scanner) using BIANCA [5], with a focus on tracts with a connection link to the ACC, i.e. forceps minor, uncinate fascicle and cingulum bundle [6]. For SC, diffusion weighted MRI data (60/120 dir, b = 1000/2700 s/mm², 2.4 mm³) were resampled to 1.25 mm³, motion corrected and aligned with the structural images. Anatomically-constrained tractography with 10 million streamlines was performed based on multi-shell-multi-tissue constrained spherical deconvolution [7]. Streamline counts (normalized number of streamlines) were estimated based on streamlines traversing through the ACC (SCACC: areas 25, 33, pregenual (p)24ab, p24c, p32, subgenual (s)24 and s32 [8]) and those traversing through both, ACC areas and WM hyperintensities (SCWMH). Using ANCOVA, we examined how DG and HC differed in WM hyperintensities, SCACC as well as SCWMH. Linear regressions were performed to study the effect of particularly depressive symptoms but also the effects of age, sex, smoking status, socioeconomic status, BMI, systolic blood pressure, CRP, LDL, HbA1c and insulin intake on WM hyperintensities, SCACC and SCWMH. Results were significant at $p < .05$.

Results:

DG showed significant increased WM hyperintensity volume for forceps minor, left uncinate fasciculus and left cingulum bundle. These effects were accompanied by increased SCWMH for right area p24c as well as area p32 bilaterally, which remained significant after correcting for the majority of risk factors included here. Importantly, subjects of DG with high HbA1c values also showed an association between SC and depressive symptomatology, with a higher CES-D being related to lower SCACC passing through left areas s24 and p24ab as well as higher SCWMH passing through left area p32.

Conclusions:

The current results not only support previous studies by showing enhanced WM hyperintensities in T2DM patients [2], they also show a relation between T2DM and higher SCWMH. Importantly, in patients with increased HbA1c levels, an increased SCWMH was additionally associated with depressive symptomatology. While MDD itself has previously been related to alterations of brain structure and function within the subgenual ACC [9], the co-presence of T2DM and depressive symptomatology in the current study was particularly linked to the left pregenual ACC, i.e. area p32, involved in cognitive control of emotion [10]. Emphasizing that the results remained significant even after correction for various risk factors, the current results hint at a superadditive manifestation of the two diseases in terms of WM integrity.

Disorders of the Nervous System:

Psychiatric (eg. Depression, Anxiety, Schizophrenia) [1]

Lifespan Development:

Aging [2]

Keywords:

Affective Disorders
Aging
DISORDERS
Psychiatric Disorders
STRUCTURAL MRI
Tractography
White Matter
WHITE MATTER IMAGING - DTI, HARDI, DSI, ETC
Other - Diabetes mellitus

[1|2]Indicates the priority used for review

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No

Please indicate below if your study was a "resting state" or "task-activation" study.

Other

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Structural MRI
Diffusion MRI

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

FSL
Other, Please list - MRtrix
SPM

Provide references using author date format

[1] Naicker, K., et al., (2017), 'Type 2 Diabetes and Comorbid Symptoms of Depression and Anxiety: Longitudinal Associations With Mortality Risk', Diabetes care, Vol. 40, No. 3, 352–358.
[2] Wassenaar, T.M., et al., (2019), 'Associations between modifiable risk factors and white matter of the aging brain: Insights from diffusion tensor imaging studies', Neurobiology of aging, Vol. 80, 56–70.
[3] Caspers, S., et al., (2014), 'Studying variability in human brain aging in a population-based German cohort-rationale and design of 1000BRAINS', Frontiers in aging neuroscience, Vol. 6, 149.
[4] Radloff, L.S. (1977), 'The CES-D scale: a self-report depression scale for research in the general population', Applied Psychological Measurement, Vol. 1, 385-401.
[5] Griffanti, L., et al., (2016), 'BIANCA (Brain Intensity AbNormality Classification Algorithm): A new tool for automated segmentation of white matter hyperintensities', NeuroImage, Vol. 141, 191–205.
[6] Hua, K., et al., (2008), 'Tract probability maps in stereotaxic spaces: Analyses of white matter anatomy and tract-specific quantification', NeuroImage, Vol. 39, No. 1, 336–347.
[7] Jeurissen, B., et al. (2014), 'Multi-tissue constrained spherical deconvolution for improved analysis of multi-shell diffusion MRI data', NeuroImage, Vol. 103, 411-426.
[8] Palomero-Gallagher, N., et al., (2008), 'Cytology and receptor architecture of human anterior cingulate cortex', The Journal of comparative neurology, Vol. 508, No. 6, 906–926.
[9] Rodríguez-Cano, E., et al., (2014), 'Evidence for structural and functional abnormality in the subgenual anterior cingulate cortex in major depressive disorder', Psychological medicine, Vol. 44, No. 15, 3263–3273.
[10] Palomero-Gallagher, N., et al., (2018), 'Human Pregenual Anterior Cingulate Cortex: Structural, Functional, and Connectional Heterogeneity', Cerebral cortex (New York, N.Y. 1991), Vol. 29, No. 6, 2552-2574.