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Serum adipokine levels in multiple sclerosis patients of the same age and their association with clinical and radiological measures

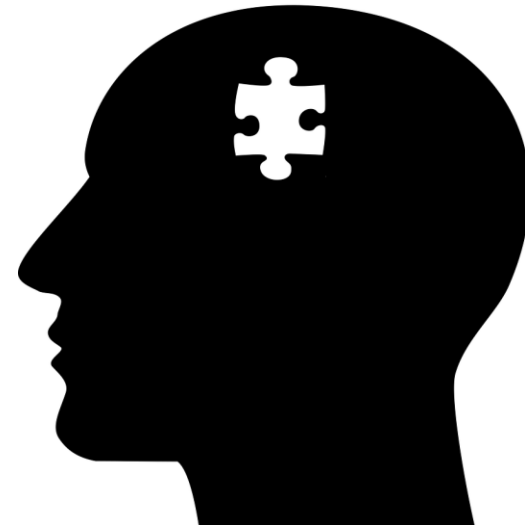
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Background

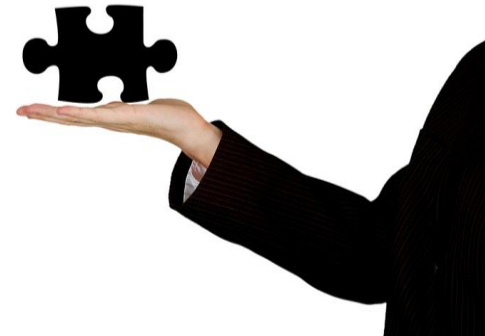
- An imbalance of pro- and anti-inflammatory adipokines, white adipose tissue hormones, is suggested to play a crucial role in the immunopathology of MS
- Correlations with MS phenotype remains to be elucidated
- Age affects adipokine function and synthesis





Objective

- To determine whether the levels of adiponectin (as anti-inflammatory) and leptin and resistin (as pro-inflammatory) relate to metabolic parameters, clinical disability measures and measures of neurodegeneration (brain volumes, neurofilament light and glial fibrillary acidic protein) in MS patients of the same age.





Methods

- All MS patients and healthy controls with available serum samples were selected from the cohort study Project Y
- Project Y is a population-based cross sectional birth year cohort of MS patients (year 1966) and HC (year 1965 - 1967) of the same age
- Serum adiponectin, leptin and resistin were measured using ELISA
- Brain volumes were quantified on 3T 3DT1 images using FSL after lesion filling
- Disability: EDSS, 9-hole Peg Test (9HPT) and Timed 25 Foot Walk Test (T25FWT)
- Adipokine levels were correlated with clinical measures and MRI volumes



Results

| | Healthy controls (n = 125) | All MS patients (n = 288) | RRMS (n = 170) | SPMS (n = 80) | PPMS (n = 37) |
|--|-------------------------------|------------------------------|----------------------|-------------------|-------------------|
| Age, y (SD) | 52.9 ± 1.2 | 52.9 ± 0.9 | 52.9 ± 0.9 | 53.1 ± 0.9 | 53.1 ± 0.9 |
| Female (%) | 92 (74%) | 207 (72%) | 139 (82%) | 48 (60%) | 19 (51%) |
| BMI (SD) | 25.6 ± 3.7 | 26.1 ± 4.9 | 26.6 ± 5.2 | 25.5 (4.4) | 25.4 (3.7) |
| Adiponectine, median (IQR) | 10591.7 (8416.6) | 12455.9 (7922.4) | 12293.4 (7365.7) | 13289.5 (8329.4) | 12681.1 (8071.0) |
| Leptin, median (IQR) | 31856.7 (50711.1) | 3487.1 (55344.0) | 42361.5 (61425.3) | 52378.2 (52585.1) | 27216.6 (45793.4) |
| Resistin, median (IQR) | 4789.2 (2666.0) | 4618.9 (2436.4) | 4607.5 (2670.4) | 4687. (2859.4) | 4562.3 (1791.4) |
| EDSS, median (IQR) | - | 3.75 (2.0) | 3.0 (2.0) | 6.0 (2.5) | 4.0 (2.5) |
| Disease duration since symptom onset (IQR) | - | 15.3 (15.9) | 14.2 (15.2) | 20.7 (11.5) | 8.1 (9.0) |
| Current DMT, n (%) | - | 134 (47%) | 94 (55%) | 33 (41%) | 8 (22%) |
| First line DMT | - | 90 (31%) | 68 (40%) | 19 (24%) | 2 (5%) |
| Second line DMT | - | 46 (16%) | 26 (15%) | 14 (18%) | 6 (16%) |
| DMT total duration (IQR) | - | 6.1 (9.0) | 6.4 (9.1) | 7.8 (8.8) | 1.5 (2.7) |
| Number of relapses, n (%) | - | | | | |
| < 5 relapses | - | 206 (72%) | 122 (72%) | 46 (58%) | 37 (100%) |
| >5 relapses | - | 82 (29%) | 48 (28%) | 34 (43%) | - |
| Statine use, n (%) | 1 (1%) | 12 (4%) | 4 (2%) | 6 (8%) | 2 (5%) |
| Diabetes mellitus, n (%) | 1 (1%) | 8 (3%) | 6 (5%) | 1 (1%) | 1 (3%) |

Table 1. General characteristics of MS patients and healthy controls



Results

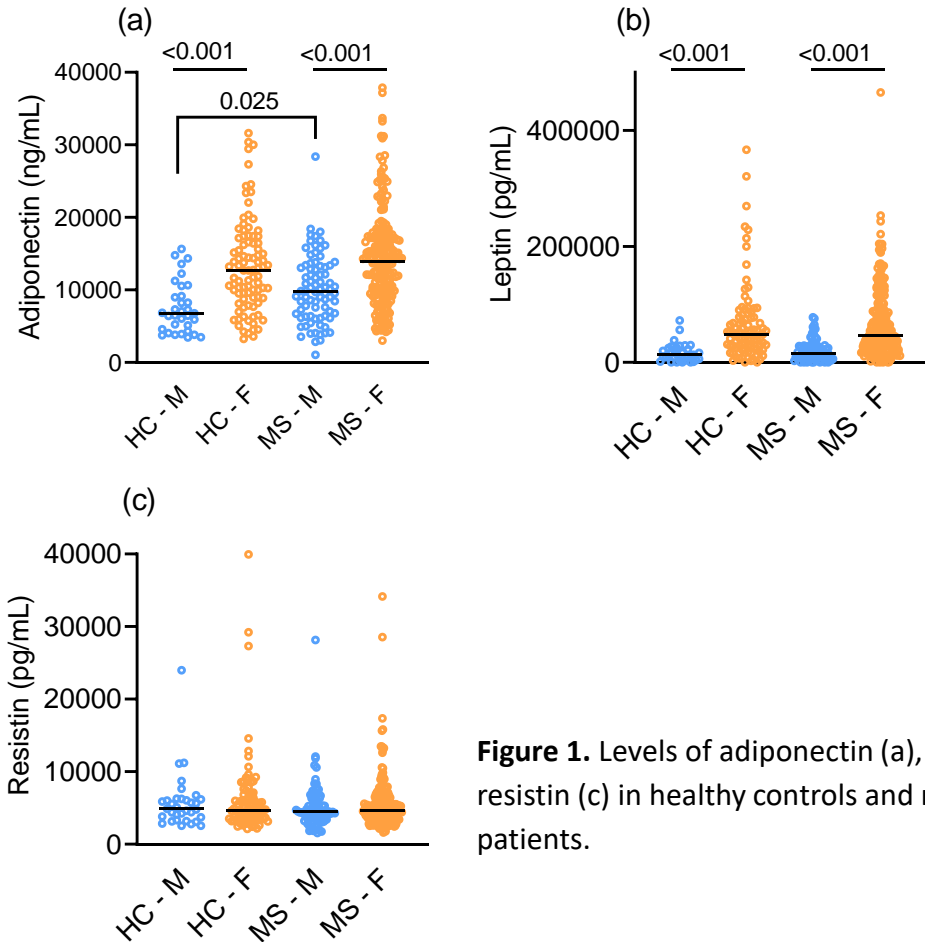


Figure 1. Levels of adiponectin (a), leptin (b) and resistin (c) in healthy controls and multiple sclerosis patients.

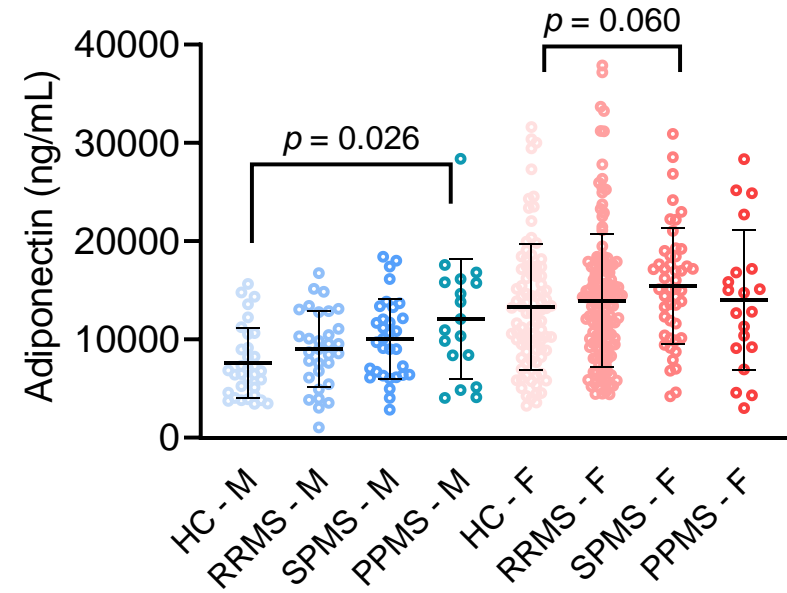


Figure 2. Adiponectin levels in healthy controls and multiple sclerosis patients, stratified by sex and MS subtype.



Results

Clinical outcome measures

- Disease duration related to
 - Adiponectin levels in female progressive patients ($\rho = 0.30$)
 - Leptin levels in female SPMS patients ($\rho = -0.45$)
- EDSS related to leptin in female RRMS ($\rho = 0.22$)
- 9HPT related to resistin in female RRMS ($\rho = -0.18$)

Neurofilament light & glial fibrillary acidic protein (GFAP)

- Higher leptin and resistin levels in female MS patients with GFAP > 90th percentile vs. female patients < 90th percentile
- GFAP related with adiponectin in male SPMS ($\rho = 0.40$)
- No associations with NfL

Results



MRI volumes

- Resistin correlated to (figure 2):
 - White matter volume ($\rho = -0.21$) in RRMS
 - Thalamic volume ($\rho = 0.41$) in SPMS
 - Total brain ($\rho = -0.44$), deep gray matter ($\rho = -0.64$), thalamic ($\rho = -0.53$), cortical gray matter ($\rho = -0.49$) and lesion volume ($\rho = 0.44$) in PPMS
- Adiponectin correlated to:
 - Total brain volume ($\rho = -0.30$) and white matter volume ($\rho = -0.36$) in SPMS

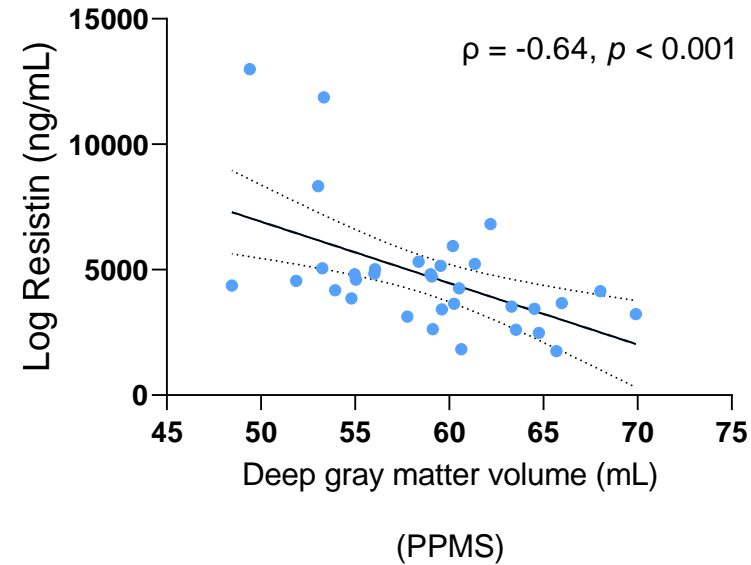


Figure 2. Correlation of resistin levels with deep gray matter volume in PPMS patients



Conclusion

- Adiponectin, leptin & resistin related to clinical outcome measures and to GFAP
- Adiponectin and resistin related to brain volumes
- Different directions of correlations suggest different effects of adipokines per phenotype (neuroprotective vs. pro-inflammatory)
- Adipokines are promising biomarkers for disease severity in MS





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