# Supplementary Tables

Table 1: Smoking, alcohol and regular physical activity information for all groups.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | Smoking | Alcohol | Sport |
| sALS | No | 49 | 97 | 88 |
|  | Quit | 32 | 8 | 10 |
|  | Yes | 31 | 7 | 14 |
| Healthy Control | No | 70 | 99 | 77 |
|  | Quit | 17 | 8 | 11 |
|  | Yes | 46 | 26 | 45 |
| DM | No | 6 | 13 | 24 |
|  | Quit | 5 | 2 | 0 |
|  | Yes | 13 | 9 | 0 |
| Healthy Control | No | 46 | 65 | 51 |
|  | Quit | 8 | 6 | 8 |
|  | Yes | 39 | 22 | 34 |
| HD | No | 10 | 8 | 9 |
|  | Quit | 10 | 13 | 9 |
|  | Yes | 1 | 0 | 3 |
| Healthy Control | No | 42 | 63 | 51 |
|  | Quit | 7 | 4 | 6 |
|  | Yes | 32 | 14 | 24 |
| SCA2 | No | 9 | 17 | 17 |
|  | Quit | 19 | 0 | 1 |
|  | Yes | 0 | 11 | 10 |
| Healthy Control | No | 51 | 71 | 54 |
|  | Quit | 9 | 4 | 10 |
|  | Yes | 36 | 21 | 32 |
| C9orf72+ ALS | No | 13 | 21 | 19 |
|  | Quit | 6 | 0 | 2 |
|  | Yes | 2 | 0 | 0 |
| Healthy Control | No | 34 | 58 | 47 |
|  | Quit | 12 | 6 | 4 |
|  | Yes | 21 | 3 | 16 |
| FA | No | 10 | 17 | 20 |
|  | Quit | 3 | 0 | 9 |
|  | Yes | 17 | 13 | 1 |
| Healthy Control | No | 31 | 31 | 24 |
|  | Quit | 3 | 2 | 7 |
|  | Yes | 18 | 19 | 21 |
| SCA1 | No | 11 | 13 | 16 |
|  | Quit | 0 | 0 | 1 |
|  | Yes | 6 | 4 | 0 |
| Healthy Control | No | 36 | 47 | 35 |
|  | Quit | 5 | 4 | 9 |
|  | Yes | 27 | 17 | 24 |

Table 2: Global levels of 5-mC in the different subtypes of ALS when compared to age- and sex-matched healthy controls without controlling for smoking, alcohol consumption and physical activity.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Patient Group | Number of Controls | Significant Increase | Patient Median | Control Median | Mann-Whitney U Test | p-value |
| sALS (n = 92) | 154 | Yes | 18.56 | 16.19 | 5430.5 | < 0.01 |
| C9orf72+ ALS (n = 18) | 84 | Yes | 24.67 | 15.98 | 338.5 | < 0.001 |
| fALS (n = 42) | 137 | Yes | 22.41 | 15.93 | 1747 | < 0.0001 |

Table 3: Comparison of global levels of 5-mC in the different patient cohorts when compared to age- and sex-matched healthy controls, correcting for smoking, alcohol consumption and physical activity.

|  |  |  |  |
| --- | --- | --- | --- |
| Disease | Number of Healthy Controls | Significant Increase | p-value |
| sALS (n = 112) | 133 | Yes | *p* < 0.01 [*F*(1, 243) = 9.159, *p* = 0.0027] |
| C9orf72+ ALS (n = 21) | 67 | Yes | *p* < 0.01 [*F*(1, 86) = 11.017, *p* = 0.0013] |
| SCA1 (n = 17) | 68 | Yes | *p* < 0.01 [*F*(1, 83) = 11.285), *p* = 0.0012] |
| SCA2 (n = 28) | 96 | Yes | *p* < 0.001 [*F*(1, 122) = 29.996, *p* = 0.0001] |
| HD (n = 21) | 81 | No | *p* > 0.1 [*F*(1, 100) = 0.193, *p* = 0.6615] |
| FRDA (n = 30) | 52 | No | *p* > 0.1 [*F*(1, 80) = 0.598, *p* = 0.4418] |
| DM1 (n = 24) | 93 | No | *p* > 0.1 [*F*(1, 115) = 0.327, *p* = 0.5686] |

Table 4: The effect of different factors on the global levels of 5-mC.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Cohort | Groups | Covariates | Significant | Statistics |
| Age of Onset | ALS | 40 and younger, 41 – 60, 61 and older | Blood Age, Disease Duration, Sex, Smoking, Alcohol, Physical Activity, Site of Onset, Consanguinity, sALS/fALS, Mutations | No | *p* > 0.1  [*F*(2, 122) = 0.123, *p* = 0.885] |
| Disease Duration | ALS | 0 – 5, 6 – 10, 11 – 20, 21 and more years | Age of Onset, Blood Age, Sex, Smoking, Alcohol, Physical Activity, Site of Onset, Consanguinity, sALS/fALS | No | *p* > 0.1  [*F*(3, 122) = 0.176, *p* = 0.913] |
| Alcohol Consumption | ALS | Yes, No, Quit | Blood Age, Disease Duration, Sex, Smoking, Physical Activity | No | *p* > 0.1  [*F*(2, 133) = 1.182, *p* = 0.310] |
| Smoking | ALS | Yes, No, Quit | Blood Age, Disease Duration, Sex, Alcohol, Physical Activity | No | *p* > 0.1  [*F*(2, 133) = 1.189, *p* = 0.308] |
| Physical Activity | ALS | Yes, No, Quit | Blood Age, Disease Duration, Sex, Alcohol, Smoking | No | *p* > 0.1  [*F*(2, 133) = 1.168, *p* = 0.314] |
| Age at Blood Collection | Healthy | 40 and younger, 41 – 60, 61 and older | Sex, Smoking, Alcohol, Physical Activity | No | *p* > 0.1  [*F*(2, 138) = 0.666, *p* = 0.666] |
| Alcohol Consumption | Healthy | Yes, No, Quit | Sex, Smoking, Age at Blood Collection, Physical Activity | Yes | *p* < 0.001  [*F*(2, 138) = 8.981, *p* = 0.000215] |
| Smoking | Healthy | Yes, No, Quit | Sex, Alcohol Consumption, Age at Blood Collection, Physical Activity | No | *p* > 0.1  [*F*(2, 138) = 1.421, *p* = 0.245] |
| Physical Activity | Healthy | Yes, No, Quit | Sex, Smoking, Age at Blood Collection, Alcohol Consumption | No | *p* > 0.1  [*F*(2, 138) = 1.862, *p* = 0.159] |