**Supplementary Table 1.**

**Effects of potential confounders on protein levels of fractalkine pathway members.**

*1a. Full Cohort*

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Fractalkine** | **CX3CR1** | **ADAM10** |
| Age (years) | r=0.046, p=0.641 | r=0.156, p=0.113 | r=-0.056, p=0.574 |
| PMI (hours) | r=-0.114, p=0.250 | r=0.080, p=0.421 | **r=-0.260, p=0.008** |
| pH | r=0.146, p=0.139 | r=0.094, p=0.342 | r=-0.146 p=0.140 |
| Storage Duration (months) | r=0.025, p=0.804 | r=0.024, p=0.808 | r=-0.018, p=0.858 |
| Body Mass Index | r=-0.014, p=0.888 | r=0.035, p=0.737 | r=-0.113, p=0.273 |
| Serum C-Reactive Protein | r=-0.059, p=0.566 | r=0.065, p=0.530 | r=0.054 p=0.603 |
| Alcohol  None/social; mean ± SD (n=59)  Moderate/heavy; mean ± SD (n=44) | 0.990 ± 0.399  0.974 ± 0.329  p=0.927 | 1.009 ± 0.168  1.002 ± 0.138  p=0.805 | 1.002 ± 0.283  0.976 ± 0.228  p=0.622 |

*1b. Psychiatric Cohort Only*

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Fractalkine** | **CX3CR1** | **ADAM10** |
| Lifetime Antipsychotic Dose (flu mg equivalent) | r=-0.158, p=0.194 | r=-0.021, p=0.864 | r=0.016, p=0.898 |
| Mood Stabilizers  No; mean ± SD (n=35)  Yes; mean ± SD (n=34) | 0.977 ± 0.161  0.982 ± 0.125  p=0.895 | 0.940 ± 0.330  1.015 ± 0.356  p=0.366 | 1.003 ± 0.268  0.950 ± 0.251  p=0.403 |
| Antidepressants  No; mean ± SD (n=41)  Yes; mean ± SD (n=28) | 0.972 ± 0.151  0.990 ± 0.134  p=0.611 | 0.945 ± 0.343  1.024 ± 0.343  p=0.356 | 1.002 ± 0.272  0.940 ± 0.240  p=0.316 |
| Suicide  No; mean ± SD (n=47)  Yes; mean ± SD (n=22) | 0.962 ± 0.141  1.016 ± 0.145  p=0.153 | 0.974 ± 0.352  0.983 ± 0.330  p=0.919 | 0.997 ± 0.272  0.934 ± 0.230  p=0.319 |
| SCZ Subtype  Undifferentiated; mean ± SD (n=)  Paranoid; mean ± SD (n=) | 0.962 ± 0.136  0.926 ± 0.208  p=0.672 | 0.925 ± 0.378  1.100 ± 0.210  p=0.124 | 0.969 ± 0.270  1.063 ± 0.307  p=0.482 |

**Supplementary Table 2.**

**Effects of potential confounders on mRNA levels of fractalkine pathway members.**

*2a. Full Cohort*

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Fractalkine** | **CX3CR1** | **ADAM10** |
| Age (years) | r=-0.106, p=0.299 | r=-0.009, p=0.929 | r=0.090, p=0.375 |
| PMI (hours) | r=-0.144, p=0.156 | r=-0.120, p=0.235 | r=0.014, p=0.892 |
| pH | r=-0.028, p=0.784 | r=0.108, p=0.286 | **r=-0.327 p=0.001** |
| RNA Integrity (RIN) | **r=-0.296, p=0.003** | r=0.090, p=0.378 | r**=-0.479 p<0.001** |
| Storage time (months) | r=-0.087, p=0.393 | r=-0.040, p=0.695 | r=-0.030, p=0.765 |
| Body Mass Index | r=0.024, p=0.821 | r=0.095, p=0.363 | r=0.088, p=0.401 |
| Serum C-Reactive Protein | r=0.040, p=0.705 | r=-0.171, p=0.104 | r=0.037, p=0.725 |
| Alcohol  None/social; mean ± SD (n=56)  Moderate/heavy; mean ± SD (n=42) | 18.763 ± 11.460  20.257 ± 13.883  p=0.500 | 1.097 ± 1.073  0.905 ± 0.818  p=0.253 | 2.549 ± 1.349  2.197 ± 0.993  p=0.594 |

*2b. Psychiatric Cohort Only*

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Fractalkine** | **CX3CR1** | **ADAM10** |
| Lifetime Antipsychotic Dose (flu mg equivalent) | r=0.164, p=0.192 | r=0.043, p=0.733 | r=0.212, p=0.090 |
| Mood Stabilizers  No; mean ± SD (n=33)  Yes; mean ± SD (n=32) | 20.540 ± 15.163  18.017 ± 11.732  p=0.454 | 1.014 ± 0.928  0.853 ± 0.637  p=0.663 | 2.435 ± 1.450  2.434 ± 1.167  p=0.431 |
| Antidepressants  No; mean ± SD (n=37)  Yes; mean ± SD (n=28) | 16.938 ± 7.470  22.416 ± 18.499  p=0.262 | 1.030 ± 0.755  0.810 ± 0.846  p=0.160 | 2.525 ± 1.476  2.314 ± 1.061  p=0.357 |
| Suicide  No; mean ± SD (n=43)  Yes; mean ± SD (n=22) | 20.468 ± 15.399  17.011 ± 8.710  p=0.362 | 0.905 ± 0.846  0.992 ± 0.705  p=0.585 | 2.531 ± 1.373  2.246 ± 1.178  p=0.373 |
| SCZ Subtype  Undifferentiated; mean ± SD (n=25)  Paranoid; mean ± SD (n=6) | 22.854 ± 16.066  11.980± 9.963  p=0.071 | 1.070 ± 0.782  1.412 ± 1.359  p=0.750 | 2.016 ± 0.675  2.465 ± 0.749  p=0.468 |

**Supplementary Figure 1: Immunoblots**



Immunoblotting yielded immunoreactive bands at ~55kDa for fractalkine (a), ~50kDa for CX3CR1 (b), and ~70kDa for ADAM10 (c) in human grey matter homogenates.

The expected molecular weight of membrane bound fractalkine is reported to be approximately 95kDa after glycosylation, with the soluble form present at approximately 80kDa. However, fractalkine has been observed at 55kDa in a number of prior studies (Fong et al., 2000; Fonović et al., 2013; Harrison et al., 1998; Hundhausen et al., 2007; Jiang et al., 2017; Lana et al., 2017). It has been suggested that this band likely reflects an alternative cleavage product, potentially via cathepsin S (Fonović et al., 2013; Hundhausen et al., 2007). Alternatively, the band may represent a degradation product of mature glycosylated fractalkine (Lucas et al., 2001) or a fractalkine precursor protein (Garton et al., 2001; Roche et al., 2017).

Validation studies revealed that the fractalkine antibody (#ab25088) recognized a recombinant human fractalkine peptide corresponding to the chemokine domain (residues 25-100). No immunoreactive band was visualized in a negative control experiment omitting the primary antibody. Specificity of this antibody has previously been validated using small interfering RNA (siRNA) knock-down of fractalkine (Morari et al., 2014), and systemic neutralization of fractalkine protein (Liu et al., 2018) in animal models.

Immunostaining for CX3CR1 and ADAM10 yielded specific bands at 50kDa and 70kDa, respectively, in agreement with prior findings (Gutwein et al., 2002; Schäfer et al., 2004) and expected molecular weights of both targets.

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