**Twin Research and Human Genetics**

**Supplementary material**

**Are the Variants of the Circle of Willis Determined by Genetic or Environmental Factors? Results of a Twin Study and Review of the Literature**

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Table S1

Variants of the anterior CW. A: ‘Normal’ variant with single, non-hypoplastic ACOA and ACAs. B: Two ACOAs. C: Unilateral ACA A1 segment hypoplasia. D: hypoplastic ACOA. E: Absent ACOA. F: Medial artery of the corpus callosum arising from the ACOA. G: Two ACOAs with medial artery of the corpus callosum arising from the distal of the ACOA.

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| --- | --- | --- | --- | --- | --- | --- | --- |
| Anterior CW variants | Variant | *n* (total) | % (total) | *n* (MZ) | % (MZ) | *n* (DZ) | % (DZ) |
| A | 54 | 45.0 | 33 | 43.4 | 21 | 47.7 |
| B | 9 | 7.5 | 6 | 7.9 | 3 | 6.8 |
| C | 6 | 5.0 | 4 | 5.2 | 2 | 4.5 |
| D | 31 | 25.8 | 19 | 25.0 | 12 | 27.3 |
| E | 13 | 10.8 | 8 | 10.5 | 5 | 11.4 |
| F | 6 | 5.0 | 5 | 6.6 | 1 | 2.3 |
| G | 1 | 0.1 | 1 | 1.3 | 0 | 0.0 |

Table S2

Variants of the posterior CW. A: ‘normal’ configuration with non-hypoplastic PCOAs present on both sides. B: PCOA hypoplasia on one side, absent contralateral PCOA. C: Unilateral fetal-type variant with ipsilateral dominant PCOA and hypoplastic PCA P1 segment. D: Unilateral fetal-type variant with absent ipsilateral PCA P1 segment and contralateral PCOA hypoplasia. E: Bilaterally absent PCOAs. F: Bilaterally hypoplastic PCOAs. G: Absent unilateral PCOA. H: Hypoplastic unilateral PCOA. I: Unilateral fetal-type variant with ipsilateral absent PCA P1 segment. J: Unilateral fetal-type variant with ipsilateral hypoplastic PCA P1 segment and contralateral hypoplastic PCOA. K: Unilateral fetal-type variant with ipsilateral hypoplastic PCA P1 segment and contralateral absent PCOA. L: Bilateral fetal-type variant with bilaterally absent PCOAs. ACA: anterior cerebral artery, ACOA: anterior communicating artery, PCA: posterior cerebral artery, PCOA: posterior communicating artery.

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| --- | --- | --- | --- | --- | --- | --- | --- |
| Posterior CW variants | Variant | *n* (total) | % (total) | *n* (MZ) | % (MZ) | *n* (DZ) | % (DZ) |
| A | 21 | 17.5 | 15 | 19.7 | 6 | 13.6 |
| B | 11 | 9.2 | 7 | 9.2 | 4 | 9.1 |
| C | 4 | 3.3 | 2 | 2.6 | 2 | 4.6 |
| D | 2 | 1.7 | 1 | 1.3 | 1 | 2.3 |
| E | 27 | 22.5 | 20 | 26.3 | 7 | 15.9 |
| F | 18 | 15.0 | 7 | 9.2 | 11 | 5.0 |
| G | 14 | 11.7 | 9 | 11.8 | 5 | 11.4 |
| H | 14 | 11.7 | 9 | 11.8 | 5 | 11.4 |
| I | 2 | 1.7 | 2 | 2.6 | 0 | 0.0 |
| J | 2 | 1.7 | 1 | 1.3 | 1 | 2.3 |
| K | 3 | 2.5 | 1 | 1.3 | 2 | 4.6 |
| L | 3 | 2.5 | 3 | 4.0 | 0 | 0.0 |

Table S3

Monozygotic discordant twins: association between the anterior and posterior CW variants and cardiovascular risk factors. BMI: body mass index, CW: Circle of Willis. *n*\* refers to the number of MZ discordant twin pairs.

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| --- | --- | --- | --- |
|  | Normal anterior or posterior CW  (*n*\*=6) | Variant anterior or posterior CW  (*n*\*=40) | p-value |
| BMI, mean±SD | 26.3±6.0 | 27.0±11.7 | 0.87 |
| Smoking, *n*(%) | 0(0.0) | 12(30.0) | 0.12 |
| Diabetes, *n*(%) | 0(0.0) | 1(2.5) | 0.70 |
| Hypertension, *n*(%) | 2(33.3) | 6(15.0) | 0.27 |
| Hypercholesterolemia, *n*(%) | 0(0.0) | 3(7.5) | 0.49 |

Table S4

Monozygotic discordant twins: intrapair comparison of transcranial Doppler parameters. *n*\* refers to the number of MZ discordant twin pairs. BA: basilar artery, LACA: left anterior cerebral artery, LMCA: left middle cerebral artery, LPCA: left posterior cerebral artery, MFV: mean flow velocity, PI: pulsatility index, RACA: right anterior cerebral artery, RMCA: right middle cerebral artery, RPCA: right posterior cerebral artery.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Total (*n*\*) | Mean±SD  Twin A | Mean±SD  Twin B | p-value |
| RMCA MFV (cm/s) | 15 | 69.1±12.5 | 67.9±15.4 | 0.72 |
| RMCA PI | 15 | 0.8±0.2 | 0.86±0.1 | 0.12 |
| RACA MFV (cm/s) | 9 | 56.9±9.1 | 48.1±5.7 | 0.04 |
| RACA PI | 9 | 0.90±0.2 | 0.94±0.2 | 0.50 |
| RPCA MFV (cm/s) | 6 | 42.2±3.3 | 44.8±6.4 | 0.42 |
| RPCA PI | 5 | 0.94±0.1 | 0.83±0.2 | 0.30 |
| LMCA MFV (cm/s) | 11 | 71.3±12.7 | 67.2±13.1 | 0.18 |
| LMCA PI | 11 | 0.83±0.2 | 0.81±0.2 | 0.70 |
| LACA MFV (cm/s) | 9 | 52.7±9.6 | 50.2±7.6 | 0.54 |
| LACA PI | 9 | 0.86±0.1 | 0.87±0.2 | 0.80 |
| LPCA MFV (cm/s) | 7 | 40.3±6.4 | 39.4±3.7 | 0.56 |
| LPCA PI | 7 | 0.93±0.2 | 0.88±0.1 | 0.34 |
| BA MFV (cm/s) | 18 | 42.6±7.1 | 43.6±8.5 | 0.63 |
| BA PI | 18 | 0.85±0.1 | 0.86±0.2 | 0.85 |