| Case | Published | Age of presentation | CPT2 activity | Genetic changes in CPT2 | Brain imaging/ autopsy data | PMG | HT | CCD | CCA | VM | BC | HC | DWM | PC | FCD | Other | NR |
|------|-----------|---------------------|---------------|------------------------|-----------------------------|-----|----|-----|-----|----|----|----|-----|----|-----|--------|----|
| 1    | Hug et al (1989) [1] | 2d | 1-17% | NR | No | + |
| 2    | Taroni F et al (1994) [2] | At birth | <15% | c.680C>T(p.Pro227Leu)/c.680C>T(p.Pro227Leu) | Yes | + |
| 3    | North et al (1995) [3] | 4d | 0-2-22% | NR | No | + |
| 4    | Land et al (1995) [4] | At birth | UD | NR | Yes | + |
| 5*   | Pierce et al (1999) [5] | 1d | NR | NR | Yes | + |
| 6    | Elpeleg et al (2001) [6] | Antenatal | UD | c.1237_1238del(p.Gln413Glufs*8);c.1342T>C(p.Phe448Leu)/c.1237_1238del(p.Gln413Glufs*8);c.1342T>C(p.Phe448Leu) | Yes | + + + |
| 7    | Elpeleg et al (2001) [6] | Antenatal | UD | c.1237_1238del(p.Gln413Glufs*8);c.1342T>C(p.Phe448Leu)/c.1237_1238del(p.Gln413Glufs*8);c.1342T>C(p.Phe448Leu) | Yes | + |
| 8    | Albers et al (2001) [7] | 17h | 6-18% | NR | Yes | + |
| 9    | Vladutiu et al (2002) [8] | 17h | 6% | c.1237_1238del(p.Gln413Glufs*8)/c.112_114delinsGCAG | No | + |
| 10   | Vekemans et al 2003 [9] | 4h | <1% | c.983A>G (p.Asp328Gly)/c.983A>G (p.Asp328Gly) | No | + |
| 11   | Vekemans et al 2003 [9] | At birth | <1% | c.983A>G (p.Asp328Gly)/c.983A>G (p.Asp328Gly) | No | + |
| 12   | Vekemans et al 2003 [9] | At birth | NR | c.983A>G (p.Asp328Gly)/c.983A>G (p.Asp328Gly) | No | + |
| 13   | Siguauke et al (2003) [10] | At birth | 7% | c.534_558del25insT(p.Leu178_Ile186delinsPhe)/c.887G>A(p.Arg296Gln) | Yes | + + |
| 14   | Smeets et al (2003) [11] | 1-10d | 2% | c.534_558del25insT (p.Leu178_Ile186delinsPhe)/g.5894G>A | No | + |
| 15   | Sharma et al (2003) [12] | Died on day 12 | 7% | NR | Yes | + |
| 16   | Isackson et al (2008) [13] | 1-2d | 9-28% | c.680C>T (p.Pro227Leu)/c.680C>T (p.Pro227Leu) | Yes | + |
| 17   | Isackson et al (2008) [13] | 1-2d | 9-28% | c.1923_1935del(p.Lys642Thrfs)/c.1923_1935del(p.Lys642Thrfs) | Yes | + |
| 18   | Isackson et al (2008) [13] | At birth | 28-58% | c.164C>G (p.Pro55Arg)/c.1782delC (Pro595fs) | Yes | + + + |
| 19   | Isackson et al (2008) [13] | 16d | 11% | c.1511C>T (p.Pro504Leu)/c.1511C>T (p.Pro504Leu) | No | + |
| 20   | Meir et al (2009) [14] | Antenatal | NR | c.1342T>C(p.Phe448Leu)/c.1342T>C(p.Phe448Leu)/c.1237_1238del(p.Gln413Glufs*8) | Yes | + |
| 21   | Meir et al (2009) [14] | Antenatal | NR | c.1342T>C(p.Phe448Leu)/c.1342T>C(p.Phe448Leu)/c.1237_1238del(p.Gln413Glufs*8) | Yes | + |
| 22   | Meir et al (2009) [14] | Antenatal | NR | c.1342T>C(p.Phe448Leu)/c.1342T>C(p.Phe448Leu)/c.1237_1238del(p.Gln413Glufs*8) | Yes | + |
| 23   | Meir et al (2009) [14] | Antenatal | NR | c.1342T>C(p.Phe448Leu)/c.1342T>C(p.Phe448Leu)/c.1237_1238del(p.Gln413Glufs*8) | Yes | + |
| 24   | Hissink-Muller et al (2009) [15] | Antenatal | NR | c.680C>T (p.Pro227Leu)/c.680C>T (p.Pro227Leu) | Yes | + |
| 25   | Yahyaoui et al (2011) [16] | 12d | NR | c.534_558del25insT(p.Leu178_Be186delinsPhe)/c.534_558del25insT(p.Leu178_Be186delinsPhe) | Yes | + + |
| 26   | Boemer et al (2016) [17] | At birth | NR | c.680C>T (p.Pro227Leu)/c.680C>T (p.Pro227Leu) | Yes | + + |
| 27   | Boemer et al (2016) [17] | At birth | 28% | c.680C>T (p.Pro227Leu)/c.680C>T (p.Pro227Leu) | Yes | + + |

*Excluded because of insufficient documentation (see Methods). NR, Not Reported; UD, Undetectable; PMG, polymicrogyria; HT, heterotopias; CCD, cerebral cystic dysplasia; CCA, corpus callosum anomaly (agenesis or dysplasia); VM, ventriculomegaly; BC, brain calcifications; HC, Hydrocephalus; DWM, Dandy-Walker malformation; PC, periventricular cysts; FCD, fetal cerebral dysgenesis. For more detailed description of cerebral anomalies please refer to source article.
Table S2. Relevant reports of the infantile form of CPT2 deficiency

| Case | Published                  | Age of presentation | CPT2 activity (% normal) | Genetic changes in CPT2                                      | Brain imaging/ autopsy data | Structural brain anomalies |
|------|----------------------------|---------------------|--------------------------|-------------------------------------------------------------|-----------------------------|---------------------------|
| 1    | Demaigre et al (1991) [18] | 3m                  | 11.0%                    | NR                                                         | No                          | NR                        |
| 2    | Taroni et al (1992) [19]   | 23m                 | 6.6-16.4%                | c.1891C>T (p.Arg631Cys)/c.1891C>T (p.Arg631Cys)             | No                          | NR                        |
| 3    | Ohtani et al (1994) [20]   | 5m                  | 37.0%                    | Frequent mutations not found                                | Brain MRI                   | NR                        |
| 4    | Vianey-Saban et al (1995)  | 40d                 | <15%                     | NR                                                         | No                          | NR                        |
| 5    | Yamamoto et al (1996) [22] | 6m                  | 3.0%                     | c.1148T>A (p.Phe383Tyr)/c.1931T>C (p.Leu644Ser)             | No                          | NR                        |
| 6    | Yamamoto et al (1996) [22] | 9m                  | 3.0%                     | c.520G>A (p.Glu174Lys)/c.1148T>A (p.Phe383Tyr)              | No                          | NR                        |
| 7    | Wataya et al (1998) [23]   | 9m                  | 6.3%                     | c.1148T>A (p.Phe383Tyr)/c.1148T>A (p.Phe383Tyr)             | No                          | NR                        |
| 8    | Fontaine et al (1998) [24] | 6w                  | 7.0%                     | NR                                                         | No                          | NR                        |
| 9*   | Yang et al (1998) [25]     | NR                  | NR                       | c.1810C>T (p.Pro604Ser)/Unknown                              | No                          | NR                        |
| 10   | Hurvitz et al (2000) [26]  | 8m                  | 16.5%                    | c.338C>T (p.Ser113Leu)/c.338C>T (p.Ser113Leu)               | No                          | NR                        |
| 11   | Vladutiu et al (2002) [8]  | 11m                 | 17.0%                    | c.1237_1238del(p.Gln413Glufs*8/c.149C>A (p.Pro50His)        | No                          | NR                        |
| 12*  | Thuillier et al (2003) [27]| NR                  | 4-12%                    | c.452G>A (p.Arg151Gln)/c.452G>A (p.Arg151Gln)              | No                          | NR                        |
| 13*  | Thuillier et al (2003) [27]| NR                  | 4-12%                    | c.983A>G (p.As p. Asp328Gly)/c.983A>G (p.As p. Asp328Gly)   | No                          | NR                        |
| 14*  | Thuillier et al (2003) [27]| NR                  | 4-12%                    | c.983A>G (p.As p. Asp328Gly)/c.983A>G (p.As p. Asp328Gly)   | No                          | NR                        |
| 15*  | Thuillier et al (2003) [27]| NR                  | 4-12%                    | c.1148T>A (p.Phe383Tyr)/Unknown                              | No                          | NR                        |
| 16*  | Thuillier et al (2003) [27]| NR                  | 4-12%                    | c.1237_1238del(p.Gln413Glufs*8)/c.1342T>C(p.Phe448Leu)/     | No                          | NR                        |
|      |                            |                     |                          | c.1237_1238del(p.Gln413Glufs*8)/c.1342T>C(p.Phe448Leu)      |                             |                           |
| 17*  | Thuillier et al (2003) [27]| NR                  | 4-12%                    | c.1883A>C (p.Tyr628Ser)/c.1883A>C (p.Tyr628Ser)             | No                          | NR                        |
| 18   | Spiegel et al (2007) [28]  | 3m                  | 3.4-7%                   | c.1507C>T (p.Arg503Cys)/c.1507C>T (p.Arg503Cys)             | No                          | NR                        |
| 19   | Isackson et al (2008) [13] | 15m                 | 2.5%                     | c.359A>G (p.Tyr120Cys)/c.359A>G (p.Tyr120Cys)                | No                          | NR                        |
| 20   | Yasuno et al (2008) [29]   | 1m                  | 18.5%                    | c.1148T>A (p.Phe383Tyr)/c.1813G>C (p.V605L)                 | No                          | NR                        |
| 21   | Yasuno et al (2008) [29]   | 2y                  | 14.4%                    | c.1148T>A (p.Phe383Tyr)/Unknown                              | No                          | NR                        |
| 22   | Yasuno et al (2008) [29]   | 6m                  | 5.6%                     | c.1148T>A (p.Phe383Tyr)/Unknown                              | No                          | NR                        |
| 23   | Yasuno et al (2008) [29]   | 11y?                | 10.0%                    | c.1148T>A (p.Phe383Tyr)/Unknown                              | No                          | NR                        |
| 24   | Hori et al (2010) [30]     | 15m                 | 14-22%                   | c.520G>A (p.Glu174Lys)/Unknown                               | Brain MRI                   | NR                        |
| 25   | Bouchireb et al (2010) [31]| 10m                 | NR                       | c.1883A>C (p.Tyr628Ser)/c.1883A>C (p.Tyr628Ser)             | Whole body MRI              | NR                        |
| 26   | Yamamotoa et al (2011) [32]| 6m                  | NR                       | c.1148T>A (p.Phe383Tyr)/c.1931T>C (p.Leu644Ser)             | No                          | NR                        |

*Excluded because of insufficient documentation (see Methods). NR-Not Reported
Table S3. Relevant reports of the late-onset adult form of CPT2 deficiency

| Published                        | Number of cases | Structural brain anomalies |
|----------------------------------|-----------------|---------------------------|
| Taggart et al (1999)[33]         | 13              | NR                        |
| Wieser et al. (2003)[34]         | 32              | NR                        |
| Isackson et al (2006)[35]        | 101             | NR                        |
| Corti et al. (2007)[36]          | 22              | NR                        |
| Anichini et al (2011)[37]        | 9*              | NR                        |
| Fanin et al. (2012)[38]          | 49              | NR                        |
| Joshi et al. (2014) [39]         | 50              | NR                        |
| **Total**                        | **276**         |                           |

* 16 other patients in this study were removed because they are also described by Fanin et al [39]. NR-Not Reported
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