# Structural Brain Volumes of Individuals at Clinical High Risk for Psychosis: A Meta-analysis

## *Supplementary Information*

# Table S1. Studies included in the meta-analyses

| Study | | Study reference | N and diagnosis | Sex (% males) | Age (years ± SD) | Included brain regions | Quality score STROBE checklist |
|---|---|---|---|---|---|---|---|
| Amygdala subnucleus volumes in psychosis high-risk state and first episode psychosis | Armio et al, 2020 | [1] | 45 CHR<br>76 HC | 56 %<br>43 % | 25.8 ± 6.1<br>27.1 ± 4.9 | CHR versus HC: amygdala, total intracranial volume | 26 |
| Regional Gray Matter Volume Abnormalities in the At Risk Mental State | Borgwardt et al, 2007 | [2] | 35 CHR<br>22 HC<br>12 CHR-T<br>23 CHR-NT | 63 %<br>59 %<br>75 %<br>57 % | 23.7 ± 5.6<br>23 ± 4.3<br>24.6 ± 5.3<br>23.3 ± 5.8 | CHR versus HC: total intracranial volume<br><br>CHR-T versus CHR-NT: total intracranial volume | 23 |
| Hippocampus abnormalities in at risk mental states for psychosis? A cross-sectional high resolution region of interest magnetic resonance imaging study | Buehlmann et al, 2010 | [3] | 37 CHR<br>22 HC<br>16 CHR-T<br>21 CHR-NT | 59 %<br>59 %<br>69 %<br>52 % | 24.7 ± 5.6<br>23 ± 4.3<br>26.4 ± 6.5<br>23.4 ± 6 | CHR versus HC: left hippocampus, right hippocampus, total hippocampus, whole brain<br><br>CHR-T versus CHR-NT: left hippocampus, right hippocampus, total hippocampus, whole brain | 24 |
| Cortical abnormalities in youth at clinical high-risk for psychosis: Findings from the NAPLS2 cohort | Chung et al, 2019 | [4] | 274 CHR<br>134 HC<br>35 CHR-T<br>239 CHR-NT | 62 %<br>54 %<br>71 %<br>61 % | 19.6 ± 4.2<br>20.5 ± 4.6<br>18.8 ± 3.8<br>19.7 ± 4.2 | CHR versus HC: cerebrospinal fluid, gray matter, lateral ventricles, left hippocampus, right hippocampus, total hippocampus, left superior temporal gyrus, right superior temporal gyrus, total superior temporal gyrus, whole brain, total intracranial volume, white matter, amygdala<br><br>CHR-T versus CHR-NT: cerebrospinal fluid , gray matter, lateral ventricles, left hippocampus, right hippocampus, total hippocampus, total intracranial volume, whole brain, white matter | 27 |
| Disorganized Gyrification Network Properties During the Transition to Psychosis | Das et al, 2018 | [5] | 79 CHR<br>44 HC | 72 %<br>39 % | 24.3 ± 5.1<br>23 ± 4.3 | CHR versus HC: total intracranial volume | 22 |
| Hippocampal Shape Abnormalities Predict Symptom Progression in Neuroleptic-Free Youth at Ultrahigh Risk for Psychosis | Dean et al, 2016 | [6] | 38 CHR<br>42 HC | 50 %<br>58 % | 18.9 ± 1.4<br>18.7 ± 1.9 | CHR versus HC: left hippocampus, right hippocampus, total hippocampus, | 27 |
| Structural and functional alterations in the brain during working memory in medication-naive patients at clinical high-risk for psychosis | Gisselgard et al, 2018 | [7] | 41 CHR<br>37 HC | 49 %<br>39 % | 16.7 ± 2.4<br>16.9 ± 3 | CHR versus HC: left hippocampus, right hippocampus, total hippocampus, total intracranial volume | 24 |
| Reduced volume in the anterior internal capsule but its maintained correlation with the frontal gray matter in subjects at ultra-high risk for psychosis | Han et al, 2012 | [8] | 43 CHR<br>42 HC | 58%<br>62% | 22.4 ± 4<br>22.8 ± 3.6 | CHR versus HC: total intracranial volume | 22 |

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|---|---|---|---|---|---|---|---|
| Caudate nucleus volume in individuals at ultra-high risk of psychosis: a cross-sectional magnetic resonance imaging study | Hannan et al, 2010 | [9] | 78 CHR<br>39 HC<br>39 CHR-T<br>19 CHR-NT | 62%<br>62%<br>62%<br>65% | 19.2 ± 3.3<br>20 ± 3.2<br>19.4 ± 3.3<br>19 ± 3.3 | CHR versus HC: lateral ventricles, whole brain<br><br>CHR-T versus CHR-NT: lateral ventricles, whole brain, total intracranial volume | 24 |
| Interrelated neuropsychological and anatomical evidence of hippocampal pathology in the at-risk mental state | Hurlemann et al, 2008 | [10] | 36 CHR<br>30 HC | 56 %<br>77 % | 27.1 ± 5.6<br>28.2 ± 6.4 | CHR versus HC: left hippocampus, right hippocampus, total hippocampus, whole brain | 22 |
| Localized gray matter volume reductions in the pars triangularis of the inferior frontal gyrus in individuals at clinical high-risk for psychosis and first episode for schizophrenia | Iwashiro et al, 2012 | [11] | 20 CHR<br>20 HC | 50 %<br>50 % | 21.4.x ± 3.6<br>22.6 ± 3.8 | CHR versus HC: total intracranial volume | 22 |
| Cortical thickness reduction in individuals at ultra-high-risk for psychosis | Jung et al, 2011 | [12] | 29 CHR<br>29 HC | 52 %<br>52 % | 22.2 ± 4.3<br>23.2 ± 2.7 | CHR versus HC: total intracranial volume | 23 |
| Symptom recovery and relationship to structure corpus callosum in individuals with an at risk mental state | Katagiri et al, 2018 | [13] | 37 CHR<br>16 HC | 30 %<br>50 % | 24.1 ± 7<br>23.2 ± 2.9 | CHR versus HC: total intracranial volume | 22 |
| Lack of Evidence for Regional Brain Volume or Cortical Thickness Abnormalities in Youths at Clinical High Risk for Psychosis: Findings From the Longitudinal Youth at Risk Study | Klauser et al, 2015 | [14] | 69 CHR<br>32 HC | 68 %<br>53 % | 21.5 ± 3.5<br>23 ± 3.9 | CHR versus HC: gray matter, bilateral hippocampus, total intracranial volume, white matter | 24 |
| Abnormal relationships between local and global brain measures in subjects at clinical high risk for psychosis: a pilot study | Konishi et al, 2018 | [15] | 19 CHR<br>20 HC | 68%<br>60 % | 20.9 ± 4.3<br>21.4 ± 3.7 | CHR versus HC: amygdala | 26 |
| Neuroanatomical correlates of executive dysfunction in the at-risk mental state for psychosis | Koutselouris et al, 2010 | [16] | 40 CHR<br>30 HC<br>11 CHR-T<br>16 CHR-NT | 68 %<br>60 %<br>82 %<br>67 % | 24.5 ± 5.9<br>26.0 ± 2.7<br>21.6 ± 3.3<br>26.0 ± 6.8 | CHR-T versus CHR-NT: total intracranial volume, white matter | 26 |
| Disease prediction in the at-risk mental state for psychosis using neuroanatomical biomarkers: results from the FePsy study | Koutselouris et al, 2012a | [17] | 37 CHR<br>22 HC<br>16 CHR-T<br>21 CHR-NT | 59%<br>59%<br>69%<br>52% | 24.7 ± 6.2<br>23 ± 4.3<br>26.4 ± 6.5<br>23.4 ±6 | CHR versus HC: Cerebrospinal fluid, total intracranial volume<br><br>CHR-T versus CHR-NT: cerebrospinal fluid, white matter, total intracranial volume | 23 |
| Multivariate patterns of brain-cognition associations relating to vulnerability and clinical outcome in the at-risk mental states for psychosis | Koutselouris et al, 2012b | [18] | 40 CHR<br>30 HC<br>11 CHR-T<br>16 CHR-NT | 68 %<br>60 %<br>82 %<br>69 % | 24.5 ± 5.8<br>26 ± 2.7<br>21.6± 3.3<br>26 ± 6.8 | CHR-T versus CHR-NT: grey matter | 23 |
| Use of neuroanatomical pattern classification to identify subjects in at-risk mental states of psychosis and predict disease transition | Koutsouleris et al, 2009 | [19] | 45 CHR<br>25 HC<br>15 CHR-T<br>18 CHR-NT | 62 %<br>44 %<br>73 %<br>61 % | 25.2 ± 5.9<br>25 ± 5.5<br>25.9 ± 6.7<br>22.4 ± 2.8 | CHR versus HC: cerebrospinal fluid, gray matter, total intracranial volume, white matter<br><br>CHR-T versus CHR-NT: cerebrospinal fluid, gray matter, total intracranial volume, white matter | 23 |

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|---|---|---|---|---|---|---|---|
| Neuroanatomical abnormalities that predate the onset of psychosis: a multicenter study | Mechelli et al, 2011 | [20] | 48 CHR-T<br>134 CHR-NT | 31 %<br>38 % | 22.7 ± 4.5<br>23.3 ± 5.3 | CHR-T versus CHR-NT: gray matter | 27 |
| Structural brain alterations in subjects at high-risk of psychosis: a voxel-based morphometric study | Meisenzahl et al, 2008 | [21] | 40 CHR<br>75 HC | 63 %<br>61 % | 25 ± 5.6<br>25.1 ± 3.8 | CHR versus HC: cerebrospinal fluid, total intracranial volume, white matter | 22 |
| Association of Adverse Outcomes With Emotion Processing and Its Neural Substrate in Individuals at Clinical High Risk for Psychosis | Modinos et al, 2020 | [22] | 213 CHR<br>52 HC<br>44 CHR-T<br>169 CHR-NT | 51 %<br>52 %<br>57 %<br>49 % | 22.9 ± 4.7<br>23.3 ± 4.0<br>22.6 ± 4.7<br>23.0 ± 4.7 | CHR versus HC: total intracranial volume<br><br>CHR-T versus CHR-NT: total intracranial volume | 25 |
| Non-reduction in hippocampal volume is associated with higher risk of psychosis | Phillips et al, 2002 | [23] | 60 CHR<br>139 HC<br>20 CHR-T<br>40 CHR-NT | 58 %<br>59 %<br>60 %<br>58 % | 20.0 ± 3.3<br>30.1 ± 12.5<br>19.6 ± 3.7<br>20.2 ± 3.1 | CHR-T versus CHR-NT: left hippocampus, right hippocampus, total hippocampus, whole brain | 27 |
| Subcortical Brain Volume Abnormalities in Individuals With an At-risk Mental State | Sabayashi et al, 2020 | [24] | 107 CHR<br>104 HC<br>21 CHR-T<br>72 CHR-NT | 46 %<br>50 %<br>36 %<br>50 % | 21.3 ± 5.4<br>22.6 ± 4.0<br>20.4 ± 4.4<br>21.7 ± 5.8 | CHR-T versus CHR-NT: total intracranial volume, lateral ventricles, left hippocampus, right hippocampus, total hippocampus | 24 |
| Brain TSPO imaging and gray matter volume in schizophrenia patients and in people at ultra high risk of psychosis: An [11C]PBR28 study. | Selvaraj et al, 2018 | [25] | 14 CHR<br>14 HC | 50 %<br>71 % | 24.3 ± 5.4<br>28.1 ± 8 | CHR versus HC: gray matter | 26 |
| Altered depth of the olfactory sulcus in ultra high-risk individuals and patients with psychotic disorders | Takahashi et al, 2014 | [26] | 135 CHR<br>87 HC<br>52 CHR-T<br>83 CHR-NT | 58 %<br>63 %<br>58 %<br>58 % | 20.1± 3.6<br>26.9 ± 10.1<br>19.6 ± 3.5<br>20.4 ± 3.6 | CHR versus HC: whole brain<br><br>CHR-T versus CHR-NT: total intracranial volume, whole brain | 24 |
| Increased pituitary volume in subjects at risk for psychosis and patients with first-episode schizophrenia | Takahashi et al, 2013 | [27] | 22 CHR<br>22 HC | 50 %<br>50 % | 19.1 ± 4.1<br>19.4 ± 4.2 | CHR versus HC:: total intracranial volume | 24 |
| Insular cortex gray matter changes in individuals at ultra-high-risk of developing psychosis | Takahashi et al, 2009a | [28] | 97 CHR<br>55 HC<br>31 CHR-T<br>66 CHR-NT | 61 %<br>65 %<br>65 %<br>59 % | 19.8 ± 3.4<br>20.8 ± 3.6<br>19.1 ± 3.6<br>20.2 ± 3.3 | CHR versus HC:: total intracranial volume<br><br>CHR-T versus CHR-NT: total intracranial volume | 25 |
| Progressive gray matter reduction of the superior temporal gyrus during transition to psychosis | Takahashi et al, 2009b | [29] | 35 CHR<br>22 HC<br>12 CHR-T<br>23 CHR-NT | 54 %<br>55 %<br>58 %<br>52 % | 20 ± 4.4<br>22 ± 4.7<br>19.5 ± 5.1<br>20.2 ± 4 | CHR versus HC: gray matter, left superior temporal gyrus, right superior temporal gyrus, total superior temporal gyrus, total intracranial volume<br><br>CHR-T versus CHR-NT: gray matter, total intracranial volume | 25 |
| Superior temporal gyrus volume in antipsychotic-naive people at risk of psychosis | Takahashi et al, 2010 | [30] | 97 CHR<br>42 HC | 61 %<br>67 % | 19.8 ± 3.4<br>20 ± 2.8 | CHR versus HC:: left superior temporal gyrus, right superior temporal gyrus, total superior temporal gyrus | 22 |
| Hippocampal Subregions Across the Psychosis Spectrum | Vargas et al, 2018 | [31] | 61 CHR<br>70 HC | 61 %<br>44 % | 18.7 ± 1.8<br>18.3 ± 2.7 | CHR versus HC:: left hippocampus, right hippocampus, total hippocampus, total intracranial volume | |
| Hippocampal subdivision and amygdalar volumes in | Witthaus et al, 2010 | [32] | 29 CHR<br>29 HC | 66 %<br>59 % | 25.3 ± 4.3<br>25.7 ± 5.2 | CHR versus HC: amygdala, left | 22 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| patients in an at-risk mental state for schizophrenia | | | | | | hippocampus, right hippocampus, total hippocampus, whole brain | |
| No evidence for structural brain changes in young adolescents at ultra high risk for psychosis | Ziermans et al, 2009 | [33] | 54 CHR<br>54 HC | 61 %<br>50 % | 15.8 ± 2.1<br>15.8 ± 1.5 | CHR versus HC: total intracranial volume, white matter, whole brain | 26 |
| Progressive structural brain changes during development of psychosis | Ziermans et al, 2012 | [34] | 43 CHR<br>30 HC<br>8 CHR-T<br>35 CHR-NT | 67 %<br>50 %<br>88 %<br>63 % | 15.6 ± 2.2<br>15.9 ± 1.4<br>16.8 ± 2.2<br>15.3 ± 2.1 | CHR versus HC: gray matter, lateral ventricles<br><br>CHR-T versus CHR-NT: gray matter, lateral ventricles, total intracranial volume, whole brain, white matter | 25 |

Note: CHR indicates Clinical high risk; HC, healthy control; CHR-T, Clinical high risk transitioned to psychosis, CHR-NT, Clinical high risk not transitioned to psychosis; SD, standard deviation.

Figure S1. PRISMA flow chart of manuscript selection

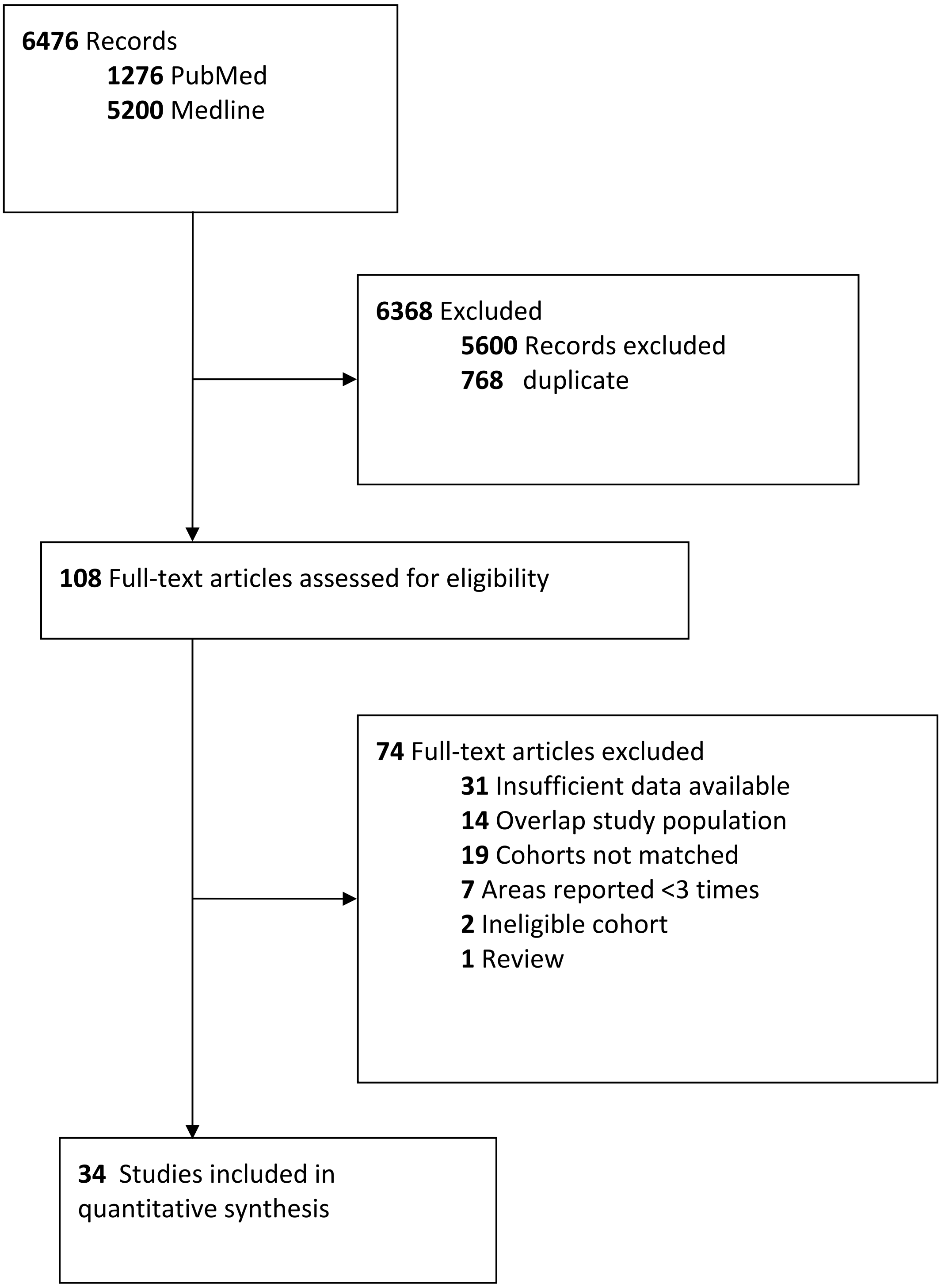


Figure S2 - Forest plot of effect sizes of studies reporting on amygdala in CHR and HC subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC |
|---|---|---|---|---|---|---|
| Armio et al, 2020 | -2.503 | -2.945 | -2.061 | 0.000 | 56 | 87 |
| Chung et al, 2019 | -0.023 | -0.191 | 0.146 | 0.793 | 415 | 201 |
| Konishi et al, 2018 | -0.475 | -1.099 | 0.149 | 0.136 | 19 | 20 |
| Witthaus et al, 2010 | 0.157 | -0.352 | 0.665 | 0.546 | 29 | 29 |
| | -0.710 | -1.907 | 0.487 | 0.245 | | |

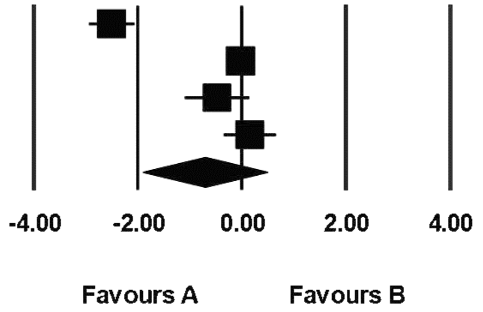



Figure S3 - Forest plot of effect sizes of studies reporting on cerebrospinal fluid volume in CHR and HC subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC |
|---|---|---|---|---|---|---|
| Chung et al, 2019 | 0.296 | 0.127 | 0.465 | 0.001 | 415 | 201 |
| Koutsouleris et al, 2009a | 0.060 | -0.424 | 0.544 | 0.808 | 45 | 25 |
| Koutsouleris et al, 2012a | 0.093 | -0.272 | 0.458 | 0.616 | 46 | 75 |
| Meisenzahl et al, 2008 | 0.021 | -0.361 | 0.402 | 0.916 | 40 | 75 |
| | 0.214 | 0.077 | 0.350 | 0.002 | | |

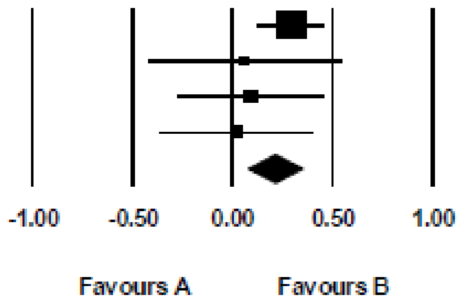



Figure S4 - Forest plot of effect sizes of studies reporting on gray matter volume in CHR and HC subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC |
|---|---|---|---|---|---|---|
| Chung et al, 2019 | -0.009 | -0.177 | 0.159 | 0.918 | 415 | 201 |
| Klauser et al, 2015 | 0.415 | -0.005 | 0.835 | 0.053 | 69 | 32 |
| Koutsouleris et al, 2009 | 0.259 | -0.227 | 0.744 | 0.296 | 45 | 25 |
| Koutsouleris et al, 2012b | 0.453 | -0.021 | 0.928 | 0.061 | 40 | 30 |
| Selvaraj et al, 2018 | -0.400 | -1.126 | 0.327 | 0.281 | 14 | 14 |
| Takahashi et al, 2009b | 0.034 | -0.492 | 0.560 | 0.898 | 35 | 22 |
| Ziermans et al, 2012 | -0.097 | -0.558 | 0.365 | 0.682 | 43 | 30 |
| | 0.106 | -0.080 | 0.292 | 0.264 | | |

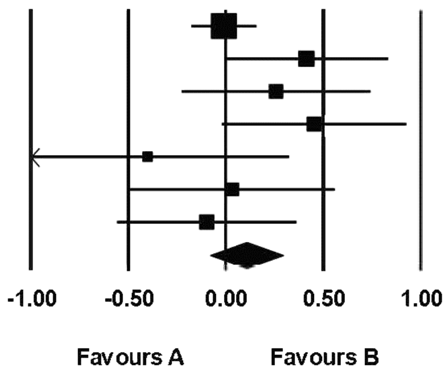


Figure S5 - Forest plot of effect sizes of studies reporting on hippocampus volume in CHR and HC subjects

| Study name | Statistics for each study | | | | | |
|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC |
| Buehlmann et al, 2010 | 0.153 | -0.368 | 0.675 | 0.565 | 37 | 22 |
| Chung et al, 2019 | -0.117 | -0.286 | 0.051 | 0.172 | 415 | 201 |
| Dean et al, 2016 | -0.495 | -0.936 | -0.054 | 0.028 | 38 | 42 |
| Gisselgard et al, 2018 | -0.467 | -0.913 | -0.021 | 0.040 | 41 | 37 |
| Hurlemann et al, 2008 | -1.142 | -1.659 | -0.625 | 0.000 | 36 | 30 |
| Klauser et al, 2015 | 0.014 | -0.402 | 0.430 | 0.948 | 69 | 32 |
| Vargas et al, 2018 | -0.068 | -0.409 | 0.273 | 0.696 | 61 | 70 |
| Witthaus et al, 2010 | -0.095 | -0.603 | 0.413 | 0.715 | 29 | 29 |
| | -0.255 | -0.488 | -0.022 | 0.032 | | |

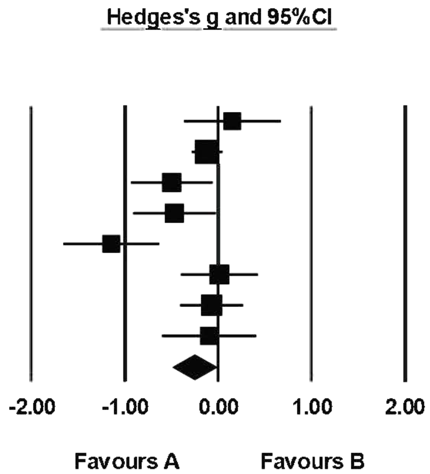



Figure S6 - Forest plot of effect sizes of studies reporting on left hippocampus volume in CHR and HC subjects

| Study name | Statistics for each study | | | | | |
|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC |
| Buehlmann et al, 2010 | 0.216 | -0.306 | 0.738 | 0.417 | 37 | 22 |
| Chung et al, 2019 | -0.109 | -0.278 | 0.059 | 0.203 | 415 | 201 |
| Dean et al, 2016 | -1.981 | -2.513 | -1.449 | 0.000 | 38 | 42 |
| Gisselgard et al, 2018 | -0.410 | -0.855 | 0.034 | 0.071 | 41 | 37 |
| Hurlemann et al, 2008 | -1.107 | -1.622 | -0.592 | 0.000 | 36 | 30 |
| Vargas et al, 2018 | -0.052 | -0.393 | 0.289 | 0.766 | 61 | 70 |
| Witthaus et al, 2010 | 0.000 | -0.508 | 0.508 | 1.000 | 29 | 29 |
| | -0.473 | -0.933 | -0.013 | 0.044 | | |

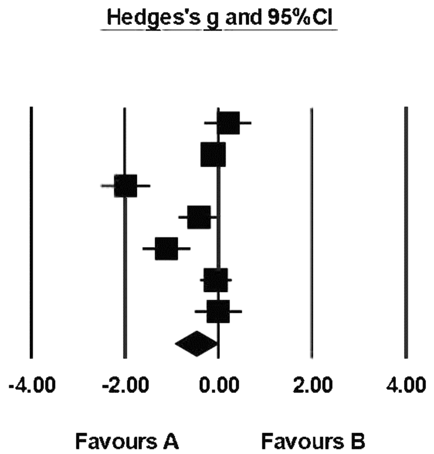



Figure S7 - Forest plot of effect sizes of studies reporting on right hippocampus volume in CHR and HC subjects

| Study name | Statistics for each study | | | | | |
|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC |
| Buehlmann et al, 2010 | 0.093 | -0.428 | 0.614 | 0.726 | 37 | 22 |
| Chung et al, 2019 | -0.129 | -0.298 | 0.039 | 0.132 | 415 | 201 |
| Dean et al, 2016 | -0.495 | -0.936 | -0.054 | 0.028 | 38 | 42 |
| Gisselgard et al, 2018 | -0.543 | -0.991 | -0.094 | 0.018 | 41 | 37 |
| Hurlemann et al, 2008 | -1.178 | -1.698 | -0.659 | 0.000 | 36 | 30 |
| Vargas et al, 2018 | -0.085 | -0.427 | 0.256 | 0.624 | 61 | 70 |
| Witthaus et al, 2010 | -0.184 | -0.693 | 0.325 | 0.479 | 29 | 29 |
| | -0.334 | -0.598 | -0.070 | 0.013 | | |

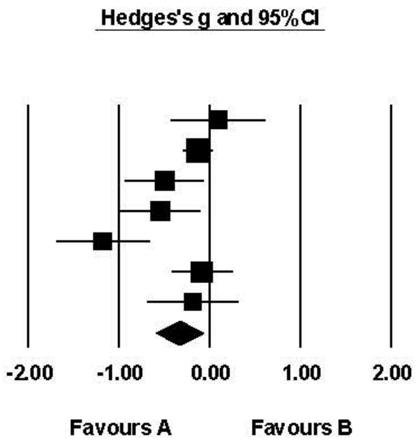


Figure S8 - Forest plot of effect sizes of studies reporting on superior temporal gyrus volume in CHR and HC subjects

| Study name | Statistics for each study | | | | | | Hedges's g and 95%CI |
|---|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | UHR | HC | |
| Chung et al, 2019 | 0.004 | -0.164 | 0.173 | 0.958 | 415 | 201 | |
| Takahashi et al, 2009b | 0.009 | -0.365 | 0.384 | 0.962 | 70 | 44 | |
| Takahashi et al, 2010 | -0.390 | -0.647 | -0.133 | 0.003 | 194 | 84 | |
| | -0.128 | -0.399 | 0.143 | 0.356 | | | |

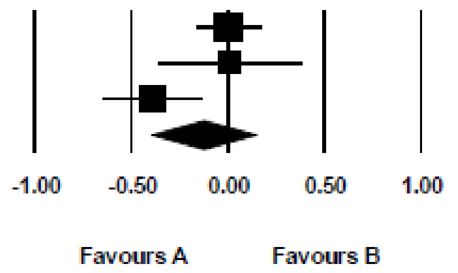



Figure S9 - Forest plot of effect sizes of studies reporting on left superior temporal gyrus volume in CHR and HC subjects

| Study name | Statistics for each study | | | | | | Hedges's g and 95%CI |
|---|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC | |
| Chung et al, 2019 | 0.033 | -0.135 | 0.201 | 0.702 | 415 | 201 | |
| Takahashi et al, 2009b | 0.027 | -0.499 | 0.553 | 0.919 | 35 | 22 | |
| Takahashi et al, 2010 | -0.513 | -0.878 | -0.148 | 0.006 | 97 | 42 | |
| | -0.146 | -0.515 | 0.224 | 0.439 | | | |

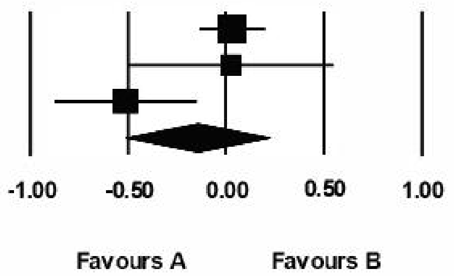



Figure S10 - Forest plot of effect sizes of studies reporting on right superior temporal gyrus volume in CHR and HC subjects

| Study name | Statistics for each study | | | | | | Hedges's g and 95%CI |
|---|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | UHR | HC | |
| Chung et al, 2019 | -0.026 | -0.195 | 0.142 | 0.758 | 415 | 201 | |
| Takahashi et al, 2009b | -0.013 | -0.539 | 0.513 | 0.961 | 35 | 22 | |
| Takahashi et al, 2010 | -0.240 | -0.601 | 0.121 | 0.193 | 97 | 42 | |
| | -0.060 | -0.207 | 0.086 | 0.418 | | | |

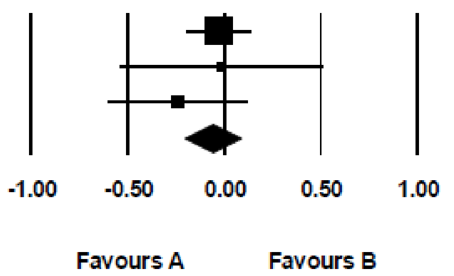


Figure S11 - Forest plot of effect sizes of studies reporting on total intracranial volume in CHR and HC subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC |
|---|---|---|---|---|---|---|
| Armio et al, 2020 | 0.012 | -0.322 | 0.346 | 0.946 | 56 | 87 |
| Borgwardt et al, 2007 | -0.045 | -0.571 | 0.481 | 0.868 | 35 | 22 |
| Chung et al, 2019 | 0.071 | -0.097 | 0.240 | 0.406 | 415 | 201 |
| Das et al, 2018 | 0.348 | -0.021 | 0.717 | 0.065 | 79 | 44 |
| Gisselgard et al, 2018 | -0.464 | -0.910 | -0.018 | 0.041 | 41 | 37 |
| Han et al, 2012 | 0.130 | -0.292 | 0.552 | 0.546 | 43 | 42 |
| Iwashiro et al, 2012 | 0.228 | -0.382 | 0.837 | 0.464 | 20 | 20 |
| Jung et al, 2011 | 0.341 | -0.171 | 0.852 | 0.192 | 29 | 29 |
| Katagiri et al, 2017 | -0.053 | -0.622 | 0.515 | 0.854 | 42 | 16 |
| Klauser et al, 2015 | 0.374 | -0.045 | 0.793 | 0.080 | 69 | 32 |
| Koutsouleris et al, 2009a | 0.169 | -0.315 | 0.653 | 0.494 | 45 | 25 |
| Koutsouleris et al, 2012a | -0.131 | -0.653 | 0.390 | 0.622 | 37 | 22 |
| Meisenzahl et al, 2008 | 0.158 | -0.224 | 0.540 | 0.417 | 40 | 75 |
| Modinos et al, 2020 | 0.001 | -0.301 | 0.304 | 0.994 | 213 | 52 |
| Takahashi et al, 2009a | -0.143 | -0.472 | 0.187 | 0.396 | 97 | 55 |
| Takahashi et al, 2009b | 2.636 | 1.921 | 3.351 | 0.000 | 35 | 22 |
| Takahashi et al, 2013 | -0.282 | -0.866 | 0.301 | 0.343 | 22 | 22 |
| Vargas et al, 2018 | 0.451 | 0.106 | 0.797 | 0.010 | 61 | 70 |
| Ziermans et al, 2009 | -0.133 | -0.508 | 0.242 | 0.486 | 54 | 54 |
| | 0.152 | -0.029 | 0.333 | 0.100 | | |

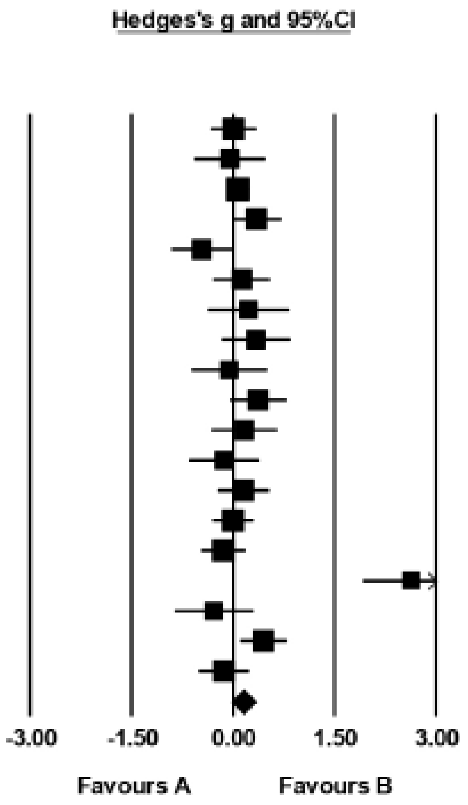



Figure S12 - Forest plot of effect sizes of studies reporting on lateral ventricles volume in CHR and HC subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC |
|---|---|---|---|---|---|---|
| Chung et al, 2019 | 0.206 | 0.038 | 0.375 | 0.016 | 415 | 201 |
| Hannan et al, 2010 | -0.007 | -0.389 | 0.374 | 0.969 | 78 | 39 |
| Ziermans et al, 2009 | 0.138 | -0.237 | 0.513 | 0.470 | 54 | 54 |
| | 0.167 | 0.024 | 0.309 | 0.022 | | |

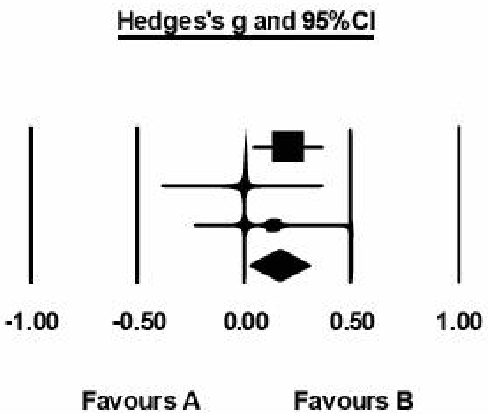


Figure S13 - Forest plot of effect sizes of studies reporting on whole brain volume in CHR and HC subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC |
|---|---|---|---|---|---|---|
| | Statistics for each study | | | | | |
| Buehlman et al, 2010 | -0.182 | -0.704 | 0.340 | 0.495 | 37 | 22 |
| Chung et al, 2019 | -0.051 | -0.219 | 0.117 | 0.551 | 415 | 201 |
| Hannan et al, 2010 | -0.338 | -0.722 | 0.046 | 0.085 | 78 | 39 |
| Hurlemann et al, 2008 | -0.160 | -0.678 | 0.359 | 0.546 | 26 | 30 |
| Takahashi et al, 2014 | -0.308 | -0.578 | -0.038 | 0.026 | 135 | 87 |
| Witthaus et al, 2010 | -0.032 | -0.536 | 0.472 | 0.901 | 30 | 29 |
| Ziermans et al, 2009 | -0.138 | -0.513 | 0.237 | 0.472 | 54 | 54 |
| | -0.144 | -0.260 | -0.028 | 0.015 | | |

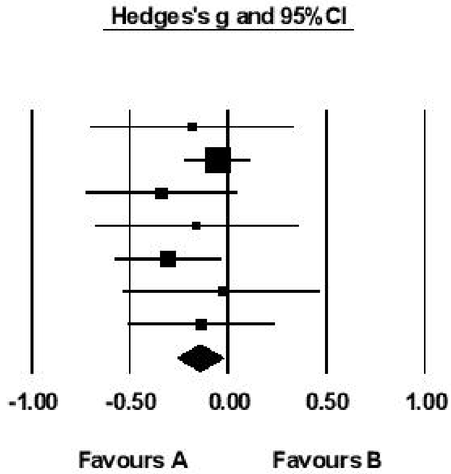



Figure S14 - Forest plot of effect sizes of studies reporting on white brain volume in CHR and HC subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR | HC |
|---|---|---|---|---|---|---|
| | Statistics for each study | | | | | |
| Chung et al, 2019 | -0.092 | -0.260 | 0.077 | 0.285 | 415 | 201 |
| Klauser et al, 2015 | 0.196 | -0.221 | 0.613 | 0.356 | 69 | 32 |
| Koutsouleris et al, 2009a | 0.099 | -0.384 | 0.583 | 0.687 | 45 | 25 |
| Meisenzahl et al, 2008 | 0.079 | -0.302 | 0.460 | 0.685 | 40 | 75 |
| Ziermans et al, 2009 | -0.067 | -0.442 | 0.307 | 0.724 | 54 | 54 |
| | -0.027 | -0.157 | 0.102 | 0.680 | | |

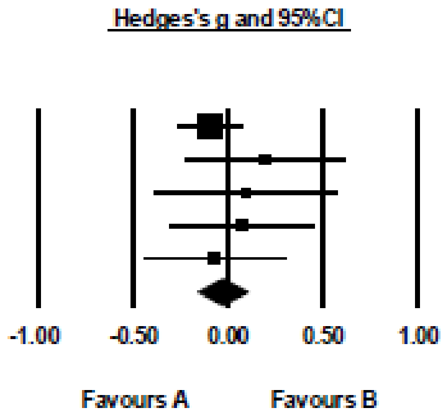



Figure S15 - Forest plot of effect sizes of studies reporting on cerebrospinal fluid volume in CHR-NT and CHR-T subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR-T | CHR-NT |
|---|---|---|---|---|---|---|
| | Statistics for each study | | | | Sample size | |
| Chung et al, 2019 | -0.236 | -0.520 | 0.047 | 0.103 | 55 | 360 |
| Koutsouleris et al, 2009a | -0.339 | -1.013 | 0.334 | 0.323 | 15 | 18 |
| Koutsouleris et al, 2012a | 0.019 | -0.618 | 0.655 | 0.954 | 16 | 21 |
| | -0.213 | -0.455 | 0.029 | 0.085 | | |

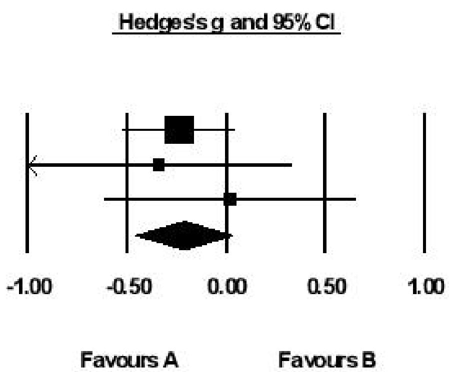


Figure S16 - Forest plot of effect sizes of studies reporting on gray matter volume in CHR-NT and CHR-T subjects

| Study name | Statistics for each study | | | | Sample size | |
|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | CHR-T | CHR-NT |
| Chung et al, 2019 | 0.033 | -0.250 | 0.316 | 0.819 | 55 | 360 |
| Koutsouleris et al, 2009 | -0.767 | -1.461 | -0.073 | 0.030 | 15 | 18 |
| Koutsouleris et al, 2012a | 0.003 | -0.633 | 0.639 | 0.992 | 16 | 21 |
| Koutsouleris et al, 2012b | 0.945 | 0.159 | 1.731 | 0.018 | 11 | 16 |
| Takahashi et al, 2009b | 0.522 | -0.171 | 1.215 | 0.140 | 12 | 23 |
| Ziermans et al, 2012 | 0.617 | -0.149 | 1.382 | 0.114 | 8 | 35 |
| | 0.188 | -0.223 | 0.599 | 0.370 | | |

Hedges's g and 95%CI

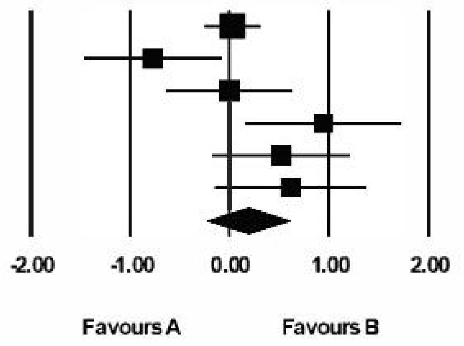



Figure S17 - Forest plot of effect sizes of studies reporting on hippocampus volume in CHR-NT and CHR-T subjects

| Study name | Statistics for each study | | | | Sample size | |
|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | CHR-T | CHR-NT |
| Buehlmann et al, 2010 | 0.061 | -0.576 | 0.697 | 0.851 | 16 | 21 |
| Chung et al, 2019 | 0.004 | -0.279 | 0.287 | 0.977 | 55 | 360 |
| Phillips et al, 2002 | 0.538 | -0.001 | 1.076 | 0.050 | 20 | 40 |
| Sasabayashi et al, 2020 | 0.044 | -0.438 | 0.526 | 0.859 | 21 | 72 |
| | 0.100 | -0.112 | 0.313 | 0.355 | | |

Hedges's g and 95% CI

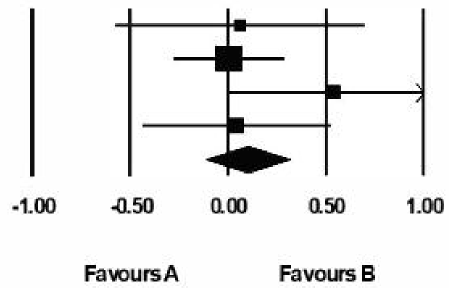



Figure S18 - Forest plot of effect sizes of studies reporting on left hippocampus volume in CHR-NT and CHR-T subjects

| Study name | Statistics for each study | | | | Sample size | |
|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | CHR-T | CHR-NT |
| Buehlmann et al, 2010 | 0.107 | -0.530 | 0.744 | 0.742 | 16 | 21 |
| Chung et al, 2019 | 0.033 | -0.250 | 0.317 | 0.818 | 55 | 360 |
| Phillips et al, 2002 | 0.739 | 0.193 | 1.285 | 0.008 | 20 | 40 |
| Sasabayashi et al, 2020 | -0.043 | -0.526 | 0.439 | 0.860 | 21 | 72 |
| | 0.175 | -0.146 | 0.496 | 0.284 | | |

Hedges's g and 95% CI

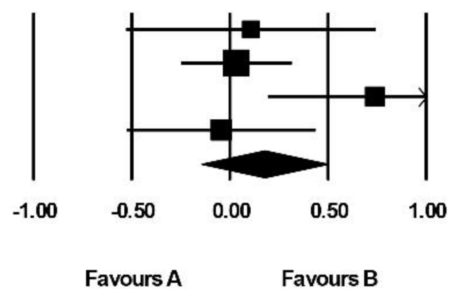


Figure S19 - Forest plot of effect sizes of studies reporting on right hippocampus volume in CHR-NT and CHR-T subjects

| Study name | Statistics for each study | | | | Sample size | |
|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | CHR-T | CHR-NT |
| Buehlmann et al, 2010 | 0.015 | -0.621 | 0.651 | 0.963 | 16 | 21 |
| Chung et al, 2019 | -0.002 | -0.285 | 0.281 | 0.990 | 55 | 360 |
| Phillips et al, 2002 | 0.356 | -0.177 | 0.890 | 0.191 | 20 | 40 |
| Sasabayashi et al, 2020 | 0.147 | -0.335 | 0.630 | 0.550 | 21 | 72 |
| | 0.083 | -0.126 | 0.293 | 0.436 | | |

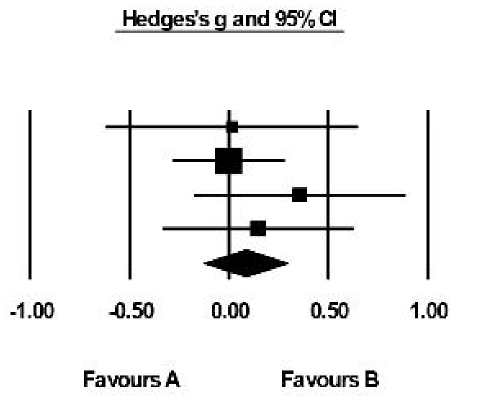



Figure S20 - Forest plot of effect sizes of studies reporting on total intracranial volume in CHR-NT and CHR-T subjects

| Study name | Statistics for each study | | | | Sample size | |
|---|---|---|---|---|---|---|
| | Hedges's g | Lower limit | Upper limit | p-Value | CHR-T | CHR-NT |
| Borgwardt et al, 2007 | 0.028 | -0.654 | 0.710 | 0.936 | 12 | 23 |
| Chung et al, 2019 | 0.064 | -0.219 | 0.347 | 0.659 | 55 | 360 |
| Hannan et al, 2010 | 0.269 | -0.172 | 0.711 | 0.232 | 39 | 39 |
| Koutsouleris et al, 2009 | -0.510 | -1.190 | 0.169 | 0.141 | 15 | 18 |
| Koutsouleris et al, 2010 | 0.474 | -0.282 | 1.229 | 0.219 | 11 | 16 |
| Koutsouleris et al, 2012a | 0.118 | -0.519 | 0.755 | 0.716 | 16 | 21 |
| Modinos et al, 2020 | -0.137 | -0.468 | 0.194 | 0.418 | 44 | 169 |
| Sabayashi et al, 2020 | -0.061 | -0.543 | 0.421 | 0.805 | 21 | 72 |
| Takahashi et al, 2009a | 0.379 | -0.047 | 0.806 | 0.081 | 31 | 66 |
| Takahashi et al, 2009b | 0.463 | -0.228 | 1.153 | 0.189 | 12 | 23 |
| Takahashi et al, 2014 | 0.074 | -0.271 | 0.419 | 0.673 | 52 | 83 |
| Ziermans et al, 2012 | 0.807 | 0.034 | 1.580 | 0.041 | 8 | 35 |
| | 0.110 | -0.039 | 0.259 | 0.148 | | |

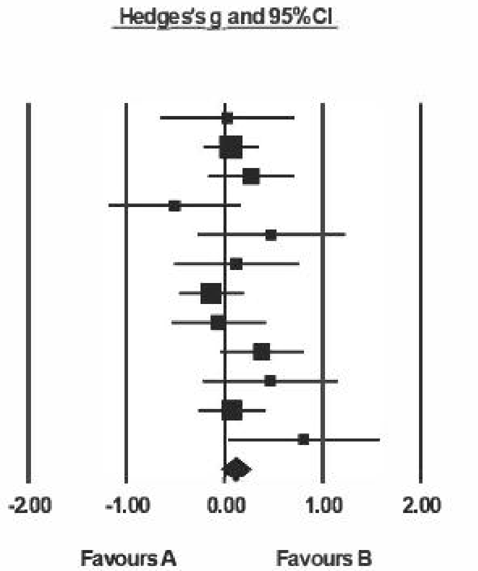


Figure S21 - Forest plot of effect sizes of studies reporting on lateral ventricles volume in CHR-NT and CHR-T subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR-T | CHR-NT |
|---|---|---|---|---|---|---|
| | Statistics for each study | | | | Sample size | |
| Chung et al, 2019 | -0.146 | -0.429 | 0.138 | 0.313 | 55 | 360 |
| Hannan et al, 2010 | -0.079 | -0.518 | 0.361 | 0.726 | 39 | 39 |
| Sasabayashi et al, 2020 | -0.241 | -0.724 | 0.242 | 0.328 | 21 | 72 |
| Ziermans et al, 2012 | 0.211 | -0.544 | 0.966 | 0.584 | 8 | 35 |
| | -0.122 | -0.328 | 0.084 | 0.245 | | |

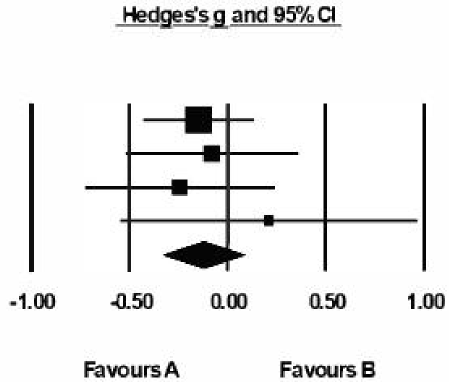



Figure S22 - Forest plot of effect sizes of studies reporting on whole brain volume in CHR-NT and CHR-T subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR-T | CHR-NT |
|---|---|---|---|---|---|---|
| | Statistics for each study | | | | Sample size | |
| Buehlman et al, 2010 | 0.100 | -0.537 | 0.737 | 0.758 | 16 | 21 |
| Chung et al, 2019 | 0.086 | -0.197 | 0.370 | 0.550 | 55 | 360 |
| Hannan et al, 2010 | 0.328 | -0.115 | 0.770 | 0.147 | 39 | 39 |
| Phillips et al, 2002 | 0.000 | -0.530 | 0.530 | 1.000 | 20 | 40 |
| Takahashi et al, 2014 | 0.066 | -0.279 | 0.410 | 0.709 | 52 | 83 |
| Ziermans et al, 2012 | 0.625 | -0.141 | 1.390 | 0.110 | 8 | 35 |
| | 0.137 | -0.035 | 0.309 | 0.119 | | |

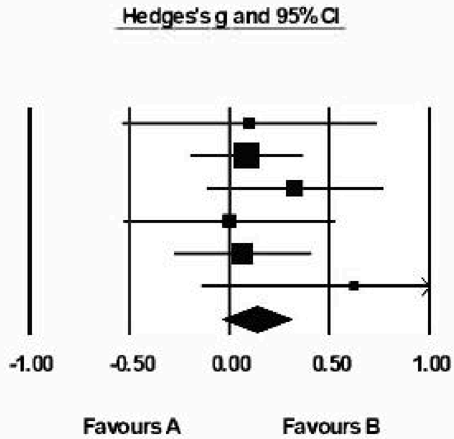
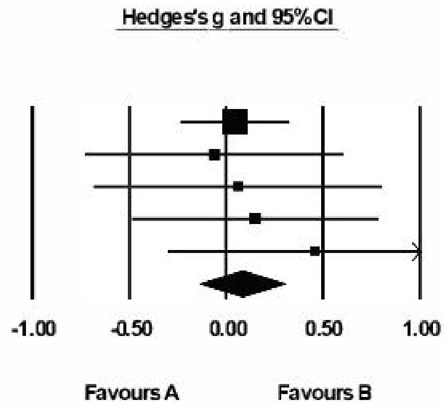



Figure S23 - Forest plot of effect sizes of studies reporting on white matter volume in CHR-NT and CHR-T subjects

| Study name | Hedges's g | Lower limit | Upper limit | p-Value | CHR-T | CHR-NT |
|---|---|---|---|---|---|---|
| | Statistics for each study | | | | Sample size | |
| Chung et al, 2019 | 0.045 | -0.238 | 0.329 | 0.753 | 55 | 360 |
| Koutsouleris et al, 2009 | -0.060 | -0.729 | 0.609 | 0.860 | 15 | 18 |
| Koutsouleris et al, 2010 | 0.061 | -0.684 | 0.806 | 0.872 | 11 | 16 |
| Koutsouleris et al, 2012a | 0.151 | -0.486 | 0.789 | 0.642 | 16 | 21 |
| Ziermans et al, 2012 | 0.459 | -0.301 | 1.219 | 0.237 | 8 | 35 |
| | 0.083 | -0.137 | 0.302 | 0.462 | | |



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