Schizophrenia Research 155 (2014) 26–30

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Schizophrenia and bipolar disorder show both common and distinct changes in cortical interneuron markers

Samantha J. Fung [a,b,c,*], Stu G. Fillman [a,b,c], Maree J. Webster [d], Cynthia Shannon Weickert [a,b,c]

[a] Schizophrenia Research Institute, Sydney, NSW, Australia
[b] Schizophrenia Research Laboratory, Neuroscience Research Australia, Sydney, Australia
[c] School of Psychiatry, University of New South Wales, Sydney, Australia
[d] Stanley Medical Research Institute, Chevy Chase, MD, USA

ARTICLE INFO

Article history:
Received 21 November 2013
Received in revised form 5 February 2014
Accepted 26 February 2014
Available online 24 March 2014

Keywords:
Somatostatin
Calbindin
Vasoactive intestinal peptide
Postmortem
mRNA

ABSTRACT

Schizophrenia and bipolar disorder are often viewed as distinct clinical disorders, however there is substantial overlap in their neuropathologies. While compromised cortical interneurons are implicated in both diseases, few studies have examined the relative contribution of the distinct interneuron populations to each psychotic disorder. We report reductions in somatostatin and vasoactive intestinal peptide mRNAs in prefrontal and orbitofrontal cortices in bipolar disorder (n = 31) and schizophrenia (n = 35) compared to controls (n = 34) and increased calbindin mRNA in schizophrenia. We show, at the molecular level, shared deficits in interneuron markers in schizophrenia and bipolar disorder, and a unique interneuron marker increase in schizophrenia.

1. Introduction

Schizophrenia and bipolar disorder may be biologically distinct or, as suggested by overlap in symptoms, genetic risk factors, and affected signaling pathways, may be on a continuum of underlying neuropathology (Craddock and Owen, 2010). Indeed, cortical interneuron pathology may be shared between individuals with schizophrenia and bipolar disorder, as GABAergic dysregulation is thought to contribute to altered gamma band oscillations and cognitive deficits in both (Hall et al., 2011; Lewis et al., 2012). Abnormalities in several cortical transcripts and proteins, including reduced glutamic acid decarboxylase 67 kDa (Akbarian et al., 1995; Guidotti et al., 2000; Volk et al., 2000; Knable et al., 2002; Torrey et al., 2005; Woo et al., 2008; Thompson et al., 2009) and various interneuron biochemical markers are found, suggesting that inhibitory neurotransmission is diminished in both schizophrenia and bipolar disorder (Benes et al., 1991; Beasley and Reynolds, 1997; Caberlotto and Hurd, 1999; Cotter et al., 2002; Hashimoto et al., 2003; Pantazopoulos et al., 2007; Hashimoto et al., 2008; Morris et al., 2008; Morris et al., 2009; Fung et al., 2010; Sibille et al., 2011; Wang et al., 2011). However, before we conclude the degree of overlap in the cortical interneuron deficit across these two clinically distinct diseases, more comparative studies using similar techniques across diagnostic groups with a wider panel of interneuron makers are needed.

Interneurons are heterogeneous cells with different subtypes inhibiting pyramidal neurons by primarily targeting the cell body and/or axon initial segment (cholecystokinin, parvalbumin), or by targeting the dendrites [e.g. somatostatin, neuropeptide Y (NPY)] (Markram et al., 2004). Interneurons may also directly inhibit other interneurons [e.g. vasoactive intestinal peptide (VIP)] (Pi et al., 2013). Thus, examining these interneuron subtypes more specifically and comparatively will determine the degree and nature of the cortical interneuron pathology in bipolar disorder and schizophrenia and will determine if they can be considered different manifestations of a similar underlying neurobiological deficit, or if they are qualitatively different.

Several previous studies have examined the expression of interneuron markers in both schizophrenia and bipolar disorder (Cotter et al., 2002; Sakai et al., 2008; Wang et al., 2011). However, whether a unique profile of interneuron deficits can be distinguished for each disorder across two functionally distinct cortical regions is unknown. We examined the relative change in expression of seven interneuron biochemical marker mRNAs (parvalbumin, cholecystokinin, somatostatin, NPY, calbindin, VIP, and calretinin) in two brain regions: the dorsolateral prefrontal cortex (DLPFC) and orbitofrontal cortex (OFC). We hypothesized there may be both shared and distinct alterations in interneuron mRNA expression in the two diseases.

* Corresponding author at: Neuroscience Research Australia, Hospital Road, Randwick, NSW 2031, Australia. Tel.: +61 2 9399 1741.
E-mail address: s.fung@neura.edu.au (S.J. Fung).

http://dx.doi.org/10.1016/j.schres.2014.02.021

2. Experimental/materials and methods

2.1. Post-mortem brain samples

Studies were carried out with approval of the University of New South Wales Human Research Ethics Committee, (#HREC07261). RNA from postmortem DLPFC (BA46) and lateral OFC cases was obtained from the Stanley Medical Research Institute Array Cohort (Table 1).

2.2. qPCR analysis

Due to availability of RNA, the examined cohort consisted of 34 controls, 31 bipolar disorder, and 35 (DLPFC) or 34 (OFC) schizophrenia subjects. cDNA was synthesized as previously described (Weickert et al., 2010). Transcript levels were measured by qPCR on ABI Prism 7900HT system using TaqMan Gene Expression Assays (Table 2) as previously described (Fung et al., 2010). The geometric mean for 4 housekeeper control mRNAs (TATA box binding protein, β-actin, ubiquitin C, β-2-microglobulin) used for normalization did not vary according to diagnostic group (DLPFC: $F = 1.51$, $df = 2, 99$, $p = 0.23$; OFC: $F = 0.53$, $df = 2, 98$, $p = 0.59$).

2.3. Analysis

Where data were not normally distributed, quantities were transformed (square root: cholecystokinin and calretinin in DLPFC, calretinin and NPY in the OFC; log: calbindin in OFC). Group outliers of >2 SD from the mean were removed (0–4 per group, average 1.57 outliers per group, 4.67%, Supplementary Table 1). Demographic variables that correlated with gene expression across the cohort (Pearson's correlation on normally distributed data, Supplementary Table 2) were used as covariates in ANCOVA analyses of differential gene expression between diagnostic groups where warranted, otherwise one-way ANOVAs were used to determine diagnostic differences (LSD post-hocs). Statistical analyses were performed using IBM SPSS Statistics, Version 20.

3. Results

3.1. Interneuron mRNAs are altered in the DLPFC of schizophrenia and bipolar disorder subjects

Several interneuron transcripts were changed in the DLPFC according to diagnostic group (Fig. 1). Somatostatin mRNA was reduced in schizophrenia (20.9%, $p = 0.021$) and in bipolar disorder (34.7%, $p < 0.001$) DLPFC relative to healthy controls (overall ANOVA, $F = 7.17$, $df = 2, 93$, $p = 0.001$). VIP was reduced 17.8% in schizophrenia subjects ($p = 0.018$) compared to controls and 32.6% in bipolar patients compared to controls ($p < 0.001$, overall ANOVA $F = 9.10$, $d = 2, 92$, $p < 0.001$). Conversely, calbindin mRNA expression was increased in people with schizophrenia relative to both controls (22.7%, $p = 0.001$) and bipolar subjects (22.5%, $p = 0.002$), and unchanged between bipolar and control subjects ($p > 0.05$, overall ANCOVA covarying for age, $F = 7.40$, $df = 2, 89$, $p = 0.001$). Parvalbumin, cholecystokinin and calretinin mRNAs did not show significant changes across diagnostic groups by ANOVA (all $F < 1.05$, $p > 0.05$). As there was a trend for overall change in NPY mRNA (ANOVA $F = 2.85$, $df = 2, 94$, $p = 0.063$) combined with our prior findings of reduced NPY mRNA in schizophrenia (Fung et al., 2010), we conducted post-hoc analysis, revealing a reduction in NPY mRNA in schizophrenia compared to controls (18.8%, $p = 0.035$), and reduced NPY mRNA in bipolar disorder relative to controls at the level of significance (17.6%, $p = 0.05$).

Table 2
TaqMan gene expression assays.

Gene name	Gene symbol	TaqMan assay ID
Interneuron marker		
Parvalbumin	PV	Hs161045_m1
Somatostatin	SST	Hs356144_m1
Calbindin	CB	Hs1077197_m1
Calretinin	CR	Hs242372_m1
Neuropeptide Y	NPY	Hs173470_m1
Cholecystokinin	CCK	Hs174937_m1
Vasoactive intestinal peptide	VIP	Hs929575_m1
Housekeeper		
TATA box binding protein	TBP	Hs00427620_m1
β-actin	ACTB	Hs99999903_m1
Ubiquitin C	UBC	Hs00824723_m1
β-2-microglobulin	B2M	Hs99999907_m1

3.2. Interneuron mRNAs are altered in the OFC of schizophrenia and bipolar disorder subjects

Somatostatin mRNA was reduced in schizophrenia (23.9%, $p = 0.004$), and in bipolar disorder relative to controls (29.9%, $p = 0.001$; overall ANOVA $F = 7.216$, $df = 2, 90$, $p = 0.001$) (Fig. 2). There was a trend for a diagnostic group difference in VIP mRNA ($F = 2.54$, $df = 2, 89$, $p = 0.085$), with reduction in bipolar relative to controls (16.2%, $p = 0.043$) and a trend toward reduction in schizophrenia relative to controls (13.6%, $p = 0.079$). Calbindin mRNA was increased in schizophrenia relative to bipolar disorder OFC (27.4%, $p = 0.016$, overall ANOVA $F = 3.33$, $df = 2, 91$, $p = 0.040$), and tended to decrease in bipolar relative to controls, but this did not quite reach statistical significance (15.3%, $p = 0.06$). No other interneuron marker mRNAs were significantly changed between groups ($F < 1.15$, $p > 0.05$).

4. Discussion

Our results indicate that bipolar disorder and schizophrenia share significant interneuron pathology, with the largest and most consistent

Table 1
Stanley array cohort demographics (based on DLPFC).

	Control group n = 34	Bipolar disorder group n = 31	Schizophrenia group n = 35
Age (years) (range)	43.8 (31–60)	44.9 (19–64)	42.6 (19–59)
Gender	9F/25M	16F/15M	9F/26M
Hemisphere	16L/18R	17L/14R	17L/18R
pH (±SD)	6.61 ± 0.27	6.46 ± 0.28	6.47 ± 0.24
PMI (hours) (±SD)	29.5 ± 13.0	36.6 ± 18.1	31.4 ± 15.4
RIN (±SD)	8.30 ± 0.69	8.32 ± 0.84	8.47 ± 0.56
Manner of death	Natural = 34	Natural = 17, suicide = 14	Natural = 28, suicide = 7
Age of onset (years) (±SD)	–	24.8 ± 8.95	21.3 ± 6.07
Duration of illness (years) (±SD)	–	20.2 ± 9.89	21.3 ± 10.1
Lifetime antipsychotics (fluphenazine equivalents, mg)	–	10,296.8 ± 23,865	85004.3 ± 100,335
Antidepressant use	Yes = 0, no = 34	Yes = 18, no = 13	Yes = 9, no = 26

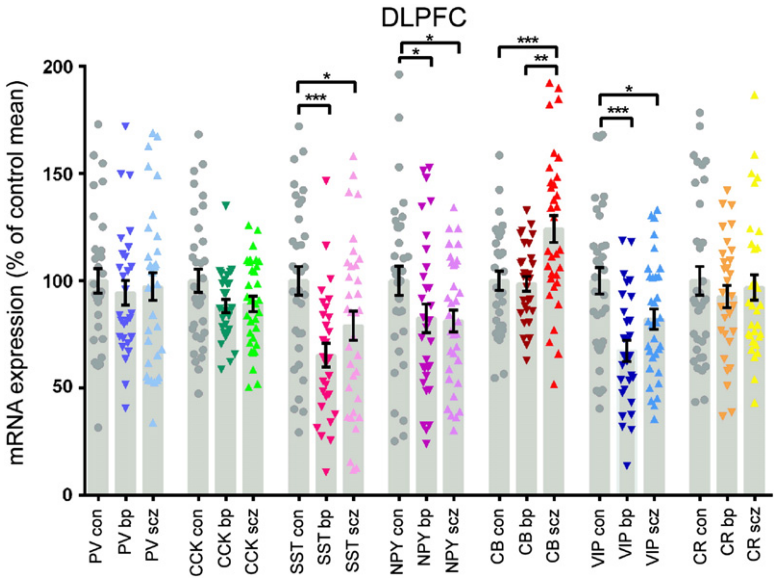

Fig. 1. Expression of interneuron marker mRNAs are altered in the dorsolateral prefrontal cortex (DLPFC) of schizophrenia (scz, light data points) and bipolar disorder (bp, dark data points) subjects compared to controls (con, gray data points). Error bars represent standard error. PV = parvalbumin, CCK = cholecystokinin, SST = somatostatin, NPY = neuropeptide Y, CB = calbindin, VIP = vasoactive intestinal peptide, CR = calretinin. *$p < 0.05$, **$p < 0.005$, ***$p < 0.001$.

reductions in VIP and somatostatin mRNAs. These abnormalities are evident across both regions studied suggesting that interneuron deficits are not restricted to the DLPFC (implicated by deficits in working memory and cognitive control), but also include the frontal cortical areas associated with social–emotional function (OFC). Our finding of reduced somatostatin, VIP and NPY mRNAs in the DLPFC in schizophrenia replicate our previous finding (Fung et al., 2010) and those of others that also show reduced somatostatin (Hashimoto et al., 2008; Morris et al., 2008) and NPY mRNA (Morris et al., 2009), implicating dendrite targeting interneurons as pathological in both psychotic disorders. A meta-analysis of microarray data comparing patients with schizophrenia and bipolar disorder with psychosis to affective disorder patients without psychosis found both somatostatin and NPY mRNAs reduced in the psychotic group, suggesting that these transcripts may be associated with psychotic features of these disorders (Choi et al., 2008). Interestingly, however, the reduction in somatostatin mRNA is of greater magnitude in bipolar disorder than schizophrenia, while psychotic and cognitive symptoms tend to be less severe in bipolar disorder (Caletti et al., 2013), suggesting additional factors also contribute to symptom severity.

Surprisingly, we found frontal cortical parvalbumin mRNA was unaltered in both schizophrenia and bipolar disorder in contrast to previous studies that consistently demonstrate reduction in parvalbumin mRNA in the cortex (Cotter et al., 2002; Hashimoto et al., 2003; Hashimoto et al., 2008; Fung et al., 2010; Sibille et al., 2011) and reductions of cell number, cell density and parvalbumin expression in hippocampus (Zhang and Reynolds, 2002; Knable et al., 2004; Konradi et al., 2011), parahippocampal region (Wang et al., 2011) and entorhinal cortex (Pantazopoulos et al., 2007). The most significantly altered mRNAs that we report in the frontal cortex (somatostatin, VIP and NPY) in schizophrenia overlap with those showing the greatest magnitude of change in our earlier report in the DLPFC (Fung et al., 2010). While our previous study also found parvalbumin mRNA reduced, the magnitude of this change was less than that of somatostatin, VIP and NPY mRNAs. This indicates that, while much attention has focused on parvalbumin

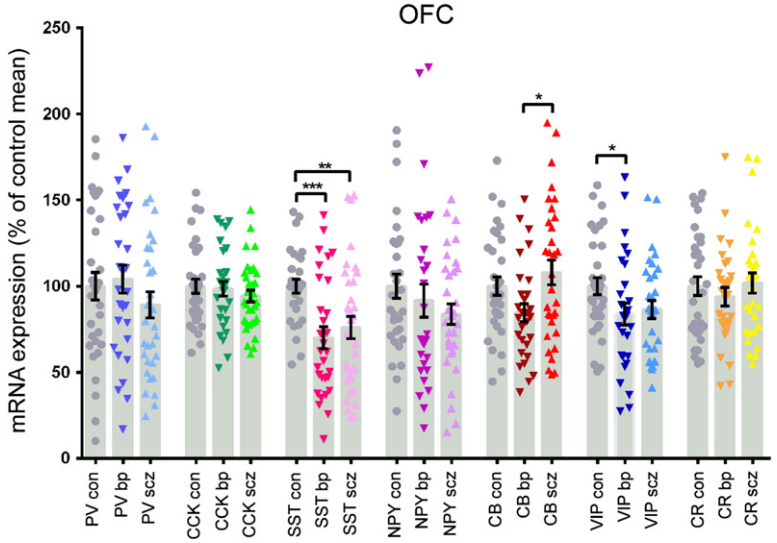

Fig. 2. Expression of interneuron marker mRNAs are altered in the orbitofrontal cortex (OFC) of schizophrenia (scz, light data points) and bipolar disorder (bp, dark data points) subjects compared to controls (con, gray data points). Error bars represent standard error. PV = parvalbumin, CCK = cholecystokinin, SST = somatostatin, NPY = neuropeptide Y, CB = calbindin, VIP = vasoactive intestinal peptide, CR = calretinin. *$p < 0.05$, **$p < 0.005$, ***$p < 0.001$.

abnormalities in schizophrenia and in animal models of schizophrenia-like behaviors, deficits in other interneuron subtypes may be more profound or widespread, at least in the frontal cortex, in schizophrenia and bipolar disorder.

We were able to identify one qualitative distinction in interneuron marker mRNA change in people with schizophrenia from those with bipolar disorder. In schizophrenia, we find increased calbindin mRNA replicating our previous finding in a different cohort (Fung et al., 2010). While calbindin may be co-expressed with somatostatin and other interneuron markers (Kawaguchi and Kubota, 1996), it can also be found in pyramidal neurons (Hof and Morrison, 1991). However, since earlier reports demonstrated an increase in density of non-pyramidal calbindin immunopositive neurons in the frontal cortex of people with schizophrenia (Daviss and Lewis, 1995), our finding of increased calbindin mRNA expression may also reflect an interneuronal increase in calbindin that may be compensatory for reductions in other interneuron markers.

Alternatively, in human frontal cortex development, calbindin mRNA expression shows a dramatic upregulation early in childhood, prior to the peak in VIP and parvalbumin mRNA expression (Fung et al., 2010). Thus, the elevated levels of calbindin mRNA that we find in schizophrenia could reflect an immature phenotype of cortical interneurons that persists into adulthood in schizophrenia, and would be consistent with the theory of delayed or arrested development of cortical interneurons in schizophrenia (Catts et al., 2013; Volk and Lewis, 2013). The increase in calbindin mRNA that we find in schizophrenia but not bipolar disorder may suggest differences in the underlying developmental trajectories of these disorders.

Our study adds to a growing body of literature suggesting that the molecular neuropathologies of schizophrenia and bipolar disorder display substantial overlap, including that much interneuron pathology is shared between the disorders and may be conserved across distinct frontal brain regions (e.g. Thompson et al., 2009; Thompson Ray et al., 2011; Sinclair et al., 2012). However an interneuron subtype-specific alteration (increase in calbindin mRNA) in the DSM-IV defined schizophrenia group only demonstrates that there are also unique differences to the interneuron pathology in these major mental illnesses and may indicate the existence of unique “biotypes” within the psychosis spectrum.

Role of funding source

This work was supported by the Schizophrenia Research Institute (utilizing infrastructure funding from the New South Wales Ministry of Health and the Macquarie Group Foundation), the University of New South Wales, and Neuroscience Research Australia. CSW is a recipient of a National Health and Medical Research Council (Australia) Senior Research Fellowship (#1021970). MJW and the brain collection are supported by the Stanley Medical Research Institute.

Contributors

SJF, MW and CSW designed the study. SJF and SGF performed the analysis and SJF wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest.

Acknowledgments

The authors acknowledge the technical support of Shan-Yuan Tsai-Chin and Duncan Sinclair.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.schres.2014.02.021.

References

Akbarian, S., Kim, J.J., Potkin, S.G., Hagman, J.O., Tafazzoli, A., Bunney Jr., W.E., Jones, E.G., 1995. Gene expression for glutamic acid decarboxylase is reduced without loss of neurons in prefrontal cortex of schizophrenics. Arch. Gen. Psychiatry 52 (4), 258–266.

Beasley, C.L., Reynolds, G.P., 1997. Parvalbumin-immunoreactive neurons are reduced in the prefrontal cortex of schizophrenics. Schizophr. Res. 24 (3), 349–355.

Benes, F.M., McSparren, J., Bird, E.D., SanGiovanni, J.P., Vincent, S.L., 1991. Deficits in small interneurons in prefrontal and cingulate cortices of schizophrenic and schizoaffective patients. Arch. Gen. Psychiatry 48 (11), 996–1001.

Caberlotto, L., Hurd, Y.L., 1999. Reduced neuropeptide Y mRNA expression in the prefrontal cortex of subjects with bipolar disorder. Neuroreport 10 (8), 1747–1750.

Caletti, E., Paoli, R.A., Fiorentini, A., Cigliobianco, M., Zugno, E., Serati, M., Orsenigo, G., Grillo, P., Zago, S., Caldiroli, A., Prunas, C., Giusti, F., Consonni, D., Altamura, A.C., 2013. Neuropsychology, social cognition and global functioning among bipolar, schizophrenic patients and healthy controls: preliminary data. Front. Hum. Neurosci. 7, 661.

Catts, V.S., Fung, S.J., Long, L.E., Joshi, D., Vercammen, A., Allen, K.M., Fillman, S.G., Rothmond, D.A., Sinclair, D., Tiwari, Y., Tsai, S.Y., Weickert, T.W., Shannon, Weickert C., 2013. Rethinking schizophrenia in the context of normal neurodevelopment. Front. Cell. Neurosci. 7, 60.

Choi, K.H., Elashoff, M., Higgs, B.W., Song, J., Kim, S., Sabunciyan, S., Diglisic, S., Yolken, R.H., Knable, M.B., Torrey, E.F., Webster, M.J., 2008. Putative psychosis genes in the prefrontal cortex: combined analysis of gene expression microarrays. BMC Psychiatry 8, 87.

Cotter, D., Landau, S., Beasley, C., Stevenson, R., Chana, G., MacMillan, L., Everall, I., 2002. The density and spatial distribution of gabaergic neurons, labelled using calcium binding proteins, in the anterior cingulate cortex in major depressive disorder, bipolar disorder, and schizophrenia. Biol. Psychiatry 51 (5), 377–386.

Craddock, N., Owen, M.J., 2010. The Kraepelinian dichotomy — going, going… but still not gone. Br. J. Psychiatry 196 (2), 92–95.

Daviss, S.R., Lewis, D.A., 1995. Local circuit neurons of the prefrontal cortex in schizophrenia: selective increase in the density of calbindin-immunoreactive neurons. Psychiatry Res. 59 (1–2), 81–96.

Fung, S.J., Webster, M.J., Sivagnanasundaram, S., Duncan, C., Elashoff, M., Weickert, C.S., 2010. Expression of interneuron markers in the dorsolateral prefrontal cortex of the developing human and in schizophrenia. Am. J. Psychiatry 167 (12), 1479–1488.

Guidotti, A., Auta, J., Davis, J.M., Di-Giorgi-Gerevini, V., Dwivedi, Y., Grayson, D.R., Impagnatiello, F., Pandey, G., Pesold, C., Sharma, R., Uzunov, D., Costa, E., 2000. Decrease in reelin and glutamic acid decarboxylase67 (GAD67) expression in schizophrenia and bipolar disorder: a postmortem brain study. Arch. Gen. Psychiatry 57 (11), 1061–1069.

Hall, M.H., Spencer, K.M., Schulze, K., McDonald, C., Kalidindi, S., Kravariti, E., Kane, F., Murray, R.M., Bramon, E., Sham, P., Rijsdijk, F., 2011. The genetic and environmental influences of event-related gamma oscillations on bipolar disorder. Bipolar Disord. 13 (3), 260–271.

Hashimoto, T., Volk, D.W., Eggan, S.M., Mirnics, K., Pierri, J.N., Sun, Z., Sampson, A.R., Lewis, D.A., 2003. Gene expression deficits in a subclass of GABA neurons in the prefrontal cortex of subjects with schizophrenia. J. Neurosci. 23 (15), 6315–6326.

Hashimoto, T., Bazmi, H.H., Mirnics, K., Wu, Q., Sampson, A.R., Lewis, D.A., 2008. Conserved regional patterns of GABA-related transcript expression in the neocortex of subjects with schizophrenia. Am. J. Psychiatry 165 (4), 479–489.

Hof, P.R., Morrison, J.H., 1991. Neocortical neuronal subpopulations labeled by a monoclonal antibody to calbindin exhibit differential vulnerability in Alzheimer's disease. Exp. Neurol. 111 (3), 293–301.

Kawaguchi, Y., Kubota, Y., 1996. Physiological and morphological identification of somatostatin- or vasoactive intestinal polypeptide-containing cells among GABAergic cell subtypes in rat frontal cortex. J. Neurosci. 16 (8), 2701–2715.

Knable, M.B., Barci, B.M., Bartko, J.J., Webster, M.J., Torrey, E.F., 2002. Molecular abnormalities in the major psychiatric illnesses: classification and regression tree (CRT) analysis of post-mortem prefrontal markers. Mol. Psychiatry 7 (4), 392–404.

Knable, M.B., Barci, B.M., Webster, M.J., Meador-Woodruff, J., Torrey, E.F., 2004. Molecular abnormalities of the hippocampus in severe psychiatric illness: postmortem findings from the stanley neuropathology consortium. Mol. Psychiatry 9 (6), 609–620 (544).

Konradi, C., Yang, C.K., Zimmerman, E.I., Lohmann, K.M., Gresch, P., Pantazopoulos, H., Berretta, S., Heckers, S., 2011. Hippocampal interneurons are abnormal in schizophrenia. Schizophr. Res. 131 (1–3), 165–173.

Lewis, D.A., Curley, A.A., Glausier, J.R., Volk, D.W., 2012. Cortical parvalbumin interneurons and cognitive dysfunction in schizophrenia. Trends Neurosci. 35 (1), 57–67.

Markram, H., Toledo-Rodriguez, M., Wang, Y., Gupta, A., Silberberg, G., Wu, C., 2004. Interneurons of the neocortical inhibitory system. Nat. Rev. Neurosci. 5 (10), 793–807.

Morris, H.M., Hashimoto, T., Lewis, D.A., 2008. Alterations in somatostatin mRNA expression in the dorsolateral prefrontal cortex of subjects with schizophrenia or schizoaffective disorder. Cereb. Cortex 18 (7), 1575–1587.

Morris, H.M., Stopczynski, R.E., Lewis, D.A., 2009. NPY mRNA expression in the prefrontal cortex: selective reduction in the superficial white matter of subjects with schizoaffective disorder. Schizophr. Res. 115 (2–3), 261–269.

Pantazopoulos, H., Lange, N., Baldessarini, R.J., Berretta, S., 2007. Parvalbumin neurons in the entorhinal cortex of subjects diagnosed with bipolar disorder or schizophrenia. Biol. Psychiatry 61 (5), 640–652.

Pi, H.J., Hangya, B., Kvitsiani, D., Sanders, J.I., Huang, Z.J., Kepecs, A., 2013. Cortical interneurons that specialize in disinhibitory control. Nature 6 (10) (ePub ahead of print).

Sakai, T., Oshima, A., Nozaki, Y., Ida, I., Haga, C., Akiyama, H., Nakazato, Y., Mikuni, M., 2008. Changes in density of calcium-binding-protein-immunoreactive GABAergic neurons in prefrontal cortex in schizophrenia and bipolar disorder. Neuropathology 28 (2), 143–150.

Sibille, E., Morris, H.M., Kota, R.S., Lewis, D.A., 2011. GABA-related transcripts in the dorsolateral prefrontal cortex in mood disorders. Int. J. Neuropsychopharmacol. 14 (6), 721–734.

Sinclair, D., Webster, M.J., Fullerton, J.M., Weickert, C.S., 2012. Glucocorticoid receptor mRNA and protein isoform alterations in the orbitofrontal cortex in schizophrenia and bipolar disorder. BMC Psychiatry 12, 84.

Thompson Ray, M., Weickert, C.S., Wyatt, E., Webster, M.J., 2011. Decreased BDNF, TrkB-TK$^+$ and GAD67 mRNA expression in the hippocampus of individuals with schizophrenia and mood disorders. J. Psychiatry Neurosci. 36 (3), 195–203.

Thompson, M., Weickert, C.S., Wyatt, E., Webster, M.J., 2009. Decreased glutamic acid decarboxylase(67) mRNA expression in multiple brain areas of patients with schizophrenia and mood disorders. J. Psychiatr. Res. 43 (11), 970–977.

Torrey, E.F., Barci, B.M., Webster, M.J., Bartko, J.J., Meador-Woodruff, J.H., Knable, M.B., 2005. Neurochemical markers for schizophrenia, bipolar disorder, and major depression in postmortem brains. Biol. Psychiatry 57 (3), 252–260.

Volk, D.W., Lewis, D.A., 2013. Prenatal ontogeny as a susceptibility period for cortical GABA neuron disturbances in schizophrenia. Neuroscience 248C, 154–164.

Volk, D.W., Austin, M.C., Pierri, J.N., Sampson, A.R., Lewis, D.A., 2000. Decreased glutamic acid decarboxylase67 messenger RNA expression in a subset of prefrontal cortical gamma-aminobutyric acid neurons in subjects with schizophrenia. Arch. Gen. Psychiatry 57 (3), 237–245.

Wang, A.Y., Lohmann, K.M., Yang, C.K., Zimmerman, E.I., Pantazopoulos, H., Herring, N., Berretta, S., Heckers, S., Konradi, C., 2011. Bipolar disorder type 1 and schizophrenia are accompanied by decreased density of parvalbumin- and somatostatin-positive interneurons in the parahippocampal region. Acta Neuropathol. 122 (5), 615–626.

Weickert, C.S., Sheedy, D., Rothmond, D.A., Dedova, I., Fung, S., Garrick, T., Wong, J., Harding, A.J., Sivagnanansundaram, S., Hunt, C., Duncan, C., Sundqvist, N., Tsai, S.Y., Anand, J., Draganic, D., Harper, C., 2010. Selection of reference gene expression in a schizophrenia brain cohort. Aust N Z J Psychiatry 44 (1), 59–70.

Woo, T.U., Shrestha, K., Lamb, D., Minns, M.M., Benes, F.M., 2008. N-methyl-D-aspartate receptor and calbindin-containing neurons in the anterior cingulate cortex in schizophrenia and bipolar disorder. Biol. Psychiatry 64 (9), 803–809.

Zhang, Z.J., Reynolds, G.P., 2002. A selective decrease in the relative density of parvalbumin-immunoreactive neurons in the hippocampus in schizophrenia. Schizophr. Res. 55 (1–2), 1–10.