Biochemical and Biophysical Research Communications 464 (2015) 76–82

Contents lists available at ScienceDirect

Biochemical and Biophysical Research Communications

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

Sgk1 regulates desmoglein 1 expression levels in oligodendrocytes in the mouse corpus callosum after chronic stress exposure

Shingo Miyata [a, *, 1], Keiko Yoshikawa [b, 1], Manabu Taniguchi [b], Toshiko Ishikawa [b], Takashi Tanaka [a], Shoko Shimizu [a], Masaya Tohyama [a, c]

[a] Division of Molecular Brain Science, Research Institute of Traditional Asian Medicine, Kinki University, Osaka-sayama, Osaka 589-8511, Japan
[b] Department of Anatomy and Neuroscience, Graduate School of Medicine, Osaka University, Suita, Osaka 565-0871, Japan
[c] Osaka Prefectural Hospital Organization, Osaka, 558-8558, Japan

ARTICLE INFO

Article history:
Received 8 May 2015
Accepted 29 May 2015
Available online 1 June 2015

Keywords:
Chronic stress
Oligodendrocytes
Sgk1
Desmosome
Major depression

ABSTRACT

Major depression, one of the most prevalent mental illnesses, is thought to be a multifactorial disease related to both genetic and environmental factors. However, the genes responsible for and the pathogenesis of major depression at the molecular level remain unclear. Recently, we reported that stressed mice with elevated plasma corticosterone levels show upregulation and activation of serum glucocorticoid-regulated kinase (Sgk1) in oligodendrocytes. Active Sgk1 causes phosphorylation of N-myc downstream-regulated gene 1 (Ndrg1), and phospho-Ndrg1 increases the expression of N-cadherin, α-catenin, and β-catenin in oligodendrocytes. This activation of the Sgk1 cascade results in morphological changes in the oligodendrocytes of nerve fiber bundles, such as those present in the corpus callosum. However, little is known about the molecular functions of the traditional and/or desmosomal cadherin superfamily in oligodendrocytes. Therefore, in this study, we aimed to elucidate the functions of the desmosomal cadherin superfamily in oligodendrocytes. Desmoglein (*Dsg*) 1, *Dsg2*, and desmocollin 1 (*Dsc1*) were found to be expressed in the corpus callosum of mouse brain, and the expression of a subtype of *Dsg1*, *Dsg1c*, was upregulated in oligodendrocytes after chronic stress exposure. Furthermore, Dsg1 proteins were localized around the plasma membrane regions of oligodendrocytes. A study in primary oligodendrocyte cultures also revealed that chronic upregulation of *Sgk1* by dexamethasone administration is involved in upregulation of *Dsg1c* mRNA. These results may indicate that chronic stress induced Sgk1 activation in oligodendrocytes, which increases Dsg1 expression near the plasma membrane. Thus, Dsg1 upregulation may be implicated in the molecular mechanisms underlying the morphological changes in oligodendrocytes in response to chronic stress exposure.

1. Introduction

Major depression is one of the most prevalent mental illnesses and is a severe psychiatric condition; it imposes a substantial burden on patients and society, such as morbidity, mortality, and economic liability [1–4]. Studies of the etiology and pathophysiology of major depression have been conducted for several decades; however, the genes responsible for and the molecular pathogenesis of major depression remain unclear. Furthermore, both genetic and environmental factors, such as repeated exposure to stress, are involved in the etiology of major depression [5–8]. Despite intensive research in these areas during recent years, the relationship between the molecular basis of chronic stress and the onset of depression is largely unknown.

Previously, we found that repeated water-immersion and restraint stress (WIRS) induces the activation of the serum glucocorticoid regulated kinase (Sgk1) in oligodendrocytes via an increase in plasma corticosterone levels [9]. We further demonstrated that Sgk1 is activated by 3-phosphoinositide-dependent protein kinase (Pdk1) and activates N-myc downstream-regulated gene 1 (Ndrg1), causing the increased expression of cadherin family proteins that are involved in the formation of adherens junctions (N-cadherin, α-catenin, and β-catenin). Thus, expression of specific adhesion molecules increases in the oligodendrocytes

* Corresponding author. Division of Molecular Brain Science, Research Institute of Traditional Asian Medicine, Kinki University, 337-2, Ohno-higashi, Osaka-sayama, Osaka 589-8511, Japan.
E-mail address: smiyata@med.kindai.ac.jp (S. Miyata).
[1] Shingo Miyata and Keiko Yoshikawa contributed equally to this work.

http://dx.doi.org/10.1016/j.bbrc.2015.05.109
0006-291X/

after repeated exposure to WIRS, but the reason for this remains unclear.

Desmoglein (Dsg) and desmocollin (Dsc) are calcium-binding transmembrane glycoprotein components of desmosomes [10–12]. Desmoplakin (Dsp) is a component of the attachment plaque of desmosomes, and binds to Dsc and keratin fibers [13]. Dsg and Dsc families are composed of 4 (Dsg1–4) and 3 (Dsc1–3) members, respectively. Furthermore, Dsg1 has three isoforms, viz., Dsg1a, b, and c [10,12]. Dsg1 belongs to the desmosomal cadherin family, and is expressed in epidermal keratinocytes as a calcium-dependent cell adhesion molecule [10–12]. However, little is known about the function of Dsg1 in the brain.

In this study, we examined the effects of WIRS on desmosomal cadherin superfamily members, such as Dsg and Dsc, as well as Dsp, in oligodendrocytes.

2. Materials and methods

2.1. Ethics statement

All animal care and handling procedures were approved by the Institutional Animal Care and Use Committee of Kinki University (No. KAME-24-021), and the Guiding Principles for the Care and Use of Laboratory Animals and the United States National Institutes of Health Guide for the Care and Use of Laboratory Animals were followed.

2.2. Animals

Adult male C57/BL6 mice weighing 25–35 g were obtained at 11 weeks of age from Japan SLC, Inc. (Hamamatsu, Japan). Three mice per cage were housed in a temperature- (22 °C ± 2 °C), humidity- (55% ± 10%), and light- (12:12-h light/dark schedule; lights on at 07:00) controlled environment and had free access to laboratory food and water. Mice were allowed to adapt to the experimental environment for 1 week before experiments were performed.

2.3. Chronic stress exposure

Mice were exposed to chronic stress as previously described [9]. Additional details are provided in the Supplementary Information.

2.4. Immunohistochemistry

Immunohistochemical analysis was performed as previously described [9,14]. Briefly, sections were immersed in pre-warmed 0.1 M citrate buffer (pH 6.0) and boiled for 5 min at 95 °C–100 °C, then allowed to cool for 20 min. The sections were then rinsed with phosphate-buffered saline (PBS) for 30 min and incubated at 4 °C for 24 h with anti-Dsg1 antibody (Santa Cruz Biotechnology, Santa Cruz, CA, USA) and anti-Olig2 antibody (Millipore, Billerica, MA, USA) diluted 1:500 in PBS. The sections were subsequently rinsed with phosphate-buffered saline (PBS) for 30 min and incubated at room temperature for 1 h with Alexa Fluor 488-conjugated goat anti-mouse IgG and 568-conjugated goat anti-rabbit IgG (Life Technologies, Carlsbad, CA, USA), diluted 1:500 in PBS. After a 1 h wash in PBS, sections were mounted on slides using PermaFluor (Thermo Scientific, Waltham, MA, USA) and visualized by confocal microscopy (LSM-510; Carl Zeiss, Oberkochen, Germany) under 20× and 40× objectives.

2.5. Immunoelectron microscopy

Immunoelectron microscopy was performed as previously described [15]. Briefly, mice were deeply anesthetized with sodium pentobarbital and perfused transcardially with 0.85% physiological saline followed by 0.05% glutaraldehyde and 4% paraformaldehyde in a 0.1 M phosphate buffer (pH 7.4). Brains were removed and post-fixed in the same fixative for 4 h at 4 °C, followed by immersion in 30% sucrose in 0.1 M phosphate buffer overnight at 4 °C. Brains sections (20 μm-thick) were then cut on a cryostat. Immunohistochemistry was performed using free-floating sections according to the ABC method. The anti-Dsg antibodies were used at a dilution of 1:100. Biotinylated anti-rabbit IgG (Vectastain Elite) was used as a secondary antibody. Immunoreactivity was visualized with 0.05% diaminobenzidine and 0.01% hydrogen peroxide in 50 mM Tris, pH 7.6. These sections were washed several times in 0.1 M phosphate buffer (pH 7.4) and after post-fixation with 1% OSO_4 for 1 h and dehydration, the sections were flat-embedded in Epon 812. Ultrathin sections were viewed without uranyl acetate or lead citrate staining, using an H-7000 electron microscope (Hitachi).

2.6. Cell culture

Primary oligodendroglial cultures were prepared from P1 Wistar rat cortex using a previously described method [14,16]. Briefly, the cortex was placed in a poly-L-lysine-coated flask in α-Minimal Essential Medium containing 10% heat-inactivated fetal bovine serum at 37 °C in an atmosphere of 95% air/5% CO_2 for 14 days with shaking at 200 rpm. Cells were then spread in poly-L-lysine-coated flasks at a density of 1×10^4 cells/cm^2 in Neurobasal Medium (Life Technologies, Inc.) containing B27 supplement, platelet-derived growth factor (PDGF), neurotrophin 3, and insulin for 3 days, after which the medium was replaced with PDGF-free Neurobasal Medium. Cells were transfected using Lipofectamine LTX, combined with Plus reagent, or Lipofectamine RNAiMAX (Life Technologies, Inc.), according to the manufacturer's instructions.

2.7. Short interfering (si)RNA knockdown

Stealth siRNA against *Sgk1* (5′-GAA GCA UUC UAU GCC GUC AAA GUU U-3′) and negative control duplexes (i.e., scrambled siRNA against *Sgk1*, 5′-GAA CUU AGU AUU GCC AAA CGC GUU U-3′) were purchased from Life Technologies Inc.

2.8. Reverse transcription and RT-PCR

Total RNA was prepared from the corpus callosum of stressed and control mice using ISOGEN (NipponGene, Toyama, Japan) according to the manufacturer's instructions. The RNA was reverse transcribed using oligo(dT)12–18 primers and SuperScript III RNaseH reverse transcriptase (Life Technologies, Inc.) according to the manufacturer's instructions. RT-PCR was performed on an ABI PRISM 7900HT Sequence Detection System using THUNDERBIRD SYBR qPCR Mix (TOYOBO CO. LTD., Osaka, Japan) according to the manufacturer's instructions. Desmosome family or *Sgk1* mRNA expression levels were normalized against *GAPDH* mRNA expression levels, as internal control. Data indicate the relative expression level as compared to internal control expression levels [17]. Additional details are provided in the Supplementary Information.

2.9. Plasmid construction

Green fluorescent protein (GFP)-fused serum/glucocorticoid-regulated kinase (Sgk1) under control of the elongation factor (EF)-1α promoter was generated using the pENTR/D-TOPO vector (Life Technologies, Inc., Carlsbad, CA, USA). Additional details are provided in the Supplementary Information.

3. Results

3.1. *Dsg1c* mRNA expression is increased in the corpus callosum after repeated exposure to WIRS

Real-time PCR analysis revealed that low but significant amounts of *Dsg1c*, *Dsg2*, and *Dsc1* mRNAs were present in the corpus callosum of mice (Fig. 1A). Among these, *Dsg2* mRNA exhibited the highest expression, followed by *Dsg1c*. In comparison, expression of *Dsc1* and *Dsc2* mRNA was very low (Fig. 1A). mRNA expression of other components of desmosomes, such as *Dsg1a*, *Dsg1b*, *Dsg3*, *Dsg4*, *Dsc3*, and *Dsp*, were absent or only present at control levels (Fig. 1A). Repeated exposure to WIRS resulted in a marked increase in *Dsg1c* mRNA expression in the corpus callosum, although no significant change was seen in the mRNA expression of other desmosomal components (Fig. 1B). Therefore, subsequent analysis focused on elucidation of the molecular mechanisms of increased *Dsg1c* expression after exposure to WIRS.

3.2. *Dsg1* expression is upregulated in oligodendrocytes after repeated exposure to WIRS

Next, we analyzed Dsg1 protein expression levels in the corpus callosum after chronic stress exposure. In accordance with real-time PCR analysis, immunohistochemical and western blotting data displayed a marked increase in Dsg1 expression also at protein level in the corpus callosum after repeated exposure to WIRS (Fig. 2A, C, D). Furthermore, Dsg1 protein was almost exclusively localized to oligodendrocytes by immunohistochemical analysis by using Olig2, an oligodendrocyte marker (Fig. 2B, arrowheads), and Dsg1 protein was localized to the plasma membranes of oligodendrocytes by immuno-electron microscopy (Fig. 2E, arrows). However, electron microscopic analysis failed to detect desmosome-like structures, e.g., keratin intermediate filaments, in oligodendrocytes (Fig. 2E).

3.3. *Sgk1* regulates *Dsg1c* mRNA expression after repeated exposure to WIRS

Previously, we demonstrated that repeated exposure to WIRS or elevated plasma corticosterone levels induced the upregulation of *Sgk1* mRNA expression in oligodendrocytes [9]. We further showed that expression of adhesion molecules involved in formation of adherens junctions, such as N-cadherin, α-catenin, and β-catenin, is increased via the Sgk1 signaling pathway [7,9]. Therefore, in this study, we examined whether Sgk1 is involved in the upregulation of *Dsg1c* expression in oligodendrocytes after repeated exposure to WIRS.

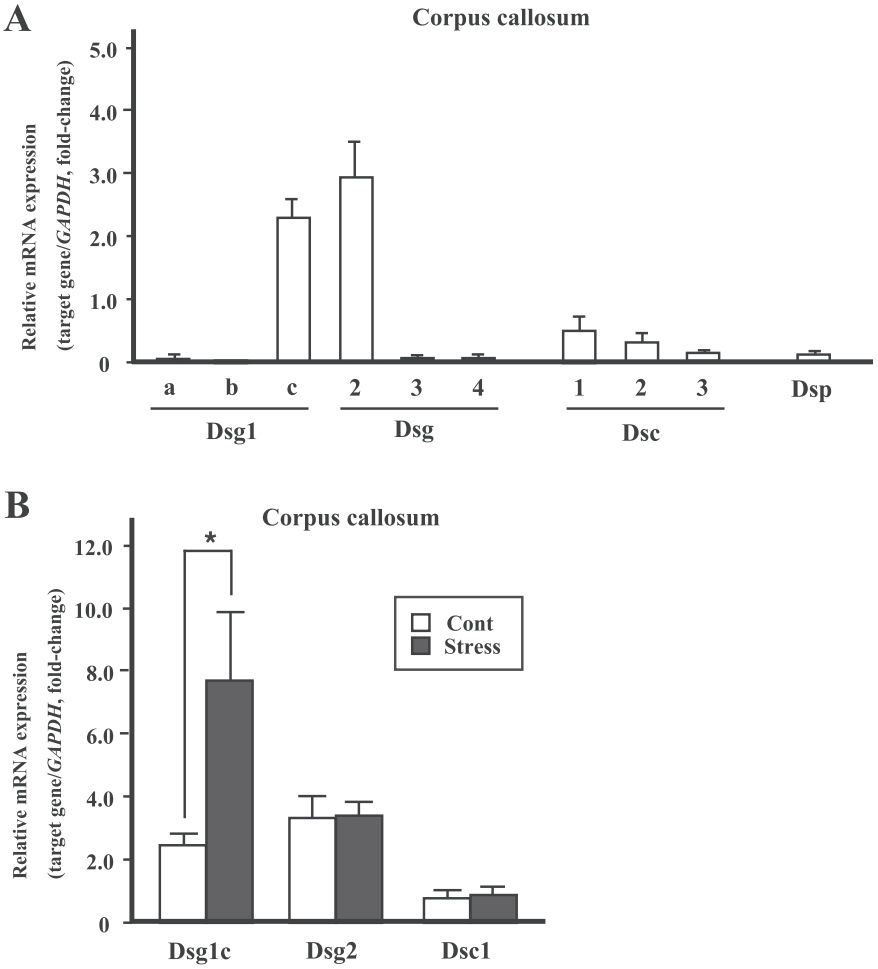

Fig. 1. Desmosomal mRNA expression in the corpus callosum and *Dsg1c* mRNA upregulation after repeated stress exposure. (A) Real-time PCR results of the expression levels of desmoglein (Dsg) 1a–c, 2–4, desmocollin (Dsc) 1–3, and desmoplakin (Dsp) mRNAs in the corpus callosum, showing the mean ± SEM of at least four independent experiments. (B) Real-time PCR results for *Dsg1c*, *Dsg2*, and *Dsc1* expression levels in the corpus callosum, showing the mean ± SEM of at least four independent experiments. Cont, control mice; Stress, chronic stress-exposed mice; $^{*}p < 0.05$, Student's *t*-test.

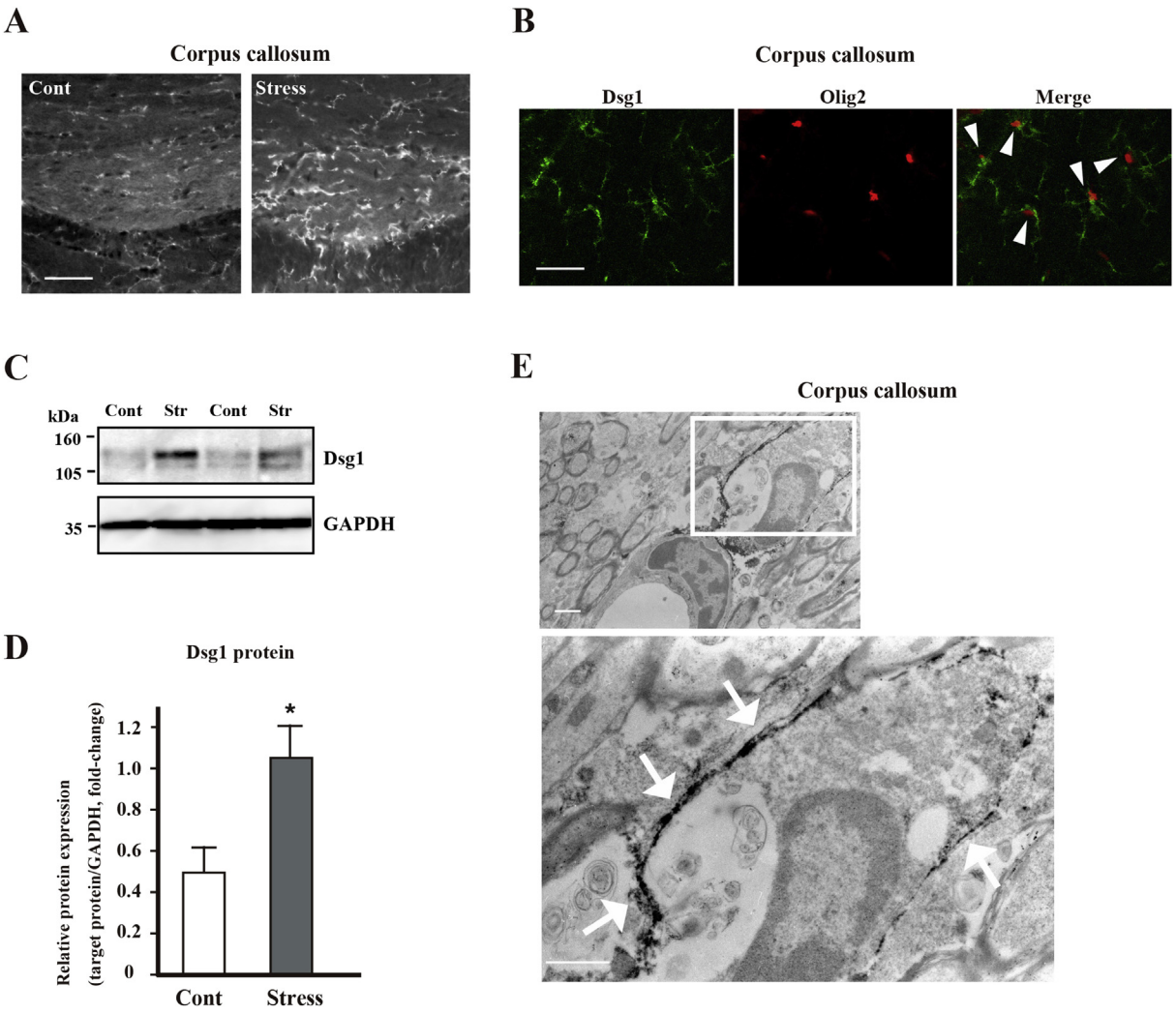

Fig. 2. Dsg1 protein expression in the plasma membrane regions of oligodendrocytes in the corpus callosum. (A) Immunohistochemical analysis of Dsg1 in the corpus callosum. Cont, control mice; Stress, chronic stress-exposed mice. Scale bar = 100 μm. (B) Immunohistochemical analysis of Dsg1 and Olig2 in the corpus callosum. Dsg1 and Olig2 merged image is shown (Arrow heads). Scale bar = 50 μm. (C) Western blot analysis of the expression of Dsg1 in the corpus callosum of control and chronically stressed mice. Cont, control mice; Str, chronic stress-exposed mice. (D) Quantification of protein bands from (C). Dsg1 protein expression levels were normalized against GAPDH expression levels. Cont, control mice; Stress, chronic stress-exposed mice. Data are expressed as mean ± SEM of at least three independent experiments. *P < 0.05, Student's *t*-test. (E) Immuno-electron microscopic analysis of Dsg1 expression in regions of the plasma membranes of oligodendrocytes. Enlargement of the squares are shown in each upper figure. Positive grains were concentrated in the plasma membrane regions (Arrows). Scale bar = 1 μm.

First, using a primary culture of rat oligodendrocytes, we compared the expression pattern of *Sgk1* and *Dsg1c* mRNAs after administration of a synthetic glucocorticoid, dexamethasone (DEX). A marked increase in *Sgk1* mRNA levels was identified immediately after DEX administration, peaking at 5 h following administration, and high expression levels of *Sgk1* mRNA were subsequently maintained at least 24 h after administration (Fig. 3A). On the other hand, no marked change was seen in *Dsg1c* mRNA until 5 h after DEX administration (Fig. 3B). However, a notable increase in *Dsg1c* mRNA expression was observed at 24 h after DEX administration (Fig. 3B).

These results indicated that *Sgk1* upregulation was prior to upregulation of *Dsg1c* mRNA expression after chronic DEX administration. Therefore, we further investigated whether *Sgk1* expression levels are involved in regulating *Dsg1c* mRNA expression in oligodendrocytes. We used RNA interference (RNAi) to knockdown endogenous *Sgk1* expression in oligodendrocytes (Fig. 4A). Knockdown of endogenous *Sgk1* failed to upregulate *Dsg1c* mRNA expression, even after DEX administration (Fig. 4B).

Furthermore, we recovered *Sgk1* expression in endogenous *Sgk1*-knockdown oligodendrocytes by overexpressing human SGK1-GFP (*Sgk1* siRNA-resistant; Fig. 4C). Overexpression of human *SGK1* resulted in upregulation of *Dsg1c* mRNA in endogenous *Sgk1*-knockdown oligodendrocytes (Fig. 4D). From these results, we concluded that *Sgk1* upregulation induced the upregulation of *Dsg1c* mRNA expression after chronic DEX administration.

4. Discussion

The present study demonstrates for the first time, both in vivo and in vitro, that repeated exposure to WIRS upregulates *Dsg1c* expression in oligodendrocytes of the corpus callosum. This occurs via increased expression of *Sgk1* due to increased plasma corticosterone levels.

However, little is known about the function of Dsg1 in the brain. In the corpus callosum of normal rat brain, we detected the presence of Dsg1c, which was localized to the oligodendrocytes. However, since other molecules related to desmosome formation, e.g.,

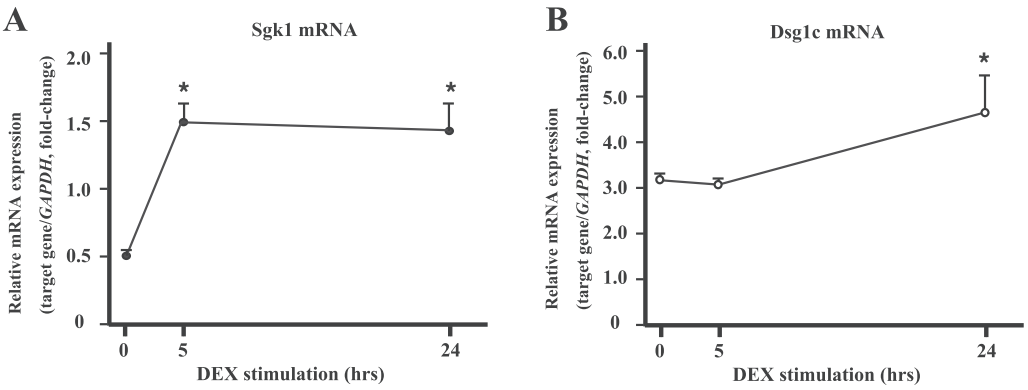

Fig. 3. Real-time PCR analysis of Sgk1 and *Dsg1c* expression in primary cultures of oligodendrocytes after chronic stress exposure. (A) Relative mRNA expression levels were determined by real-time PCR and normalized to that of *Gapdh* mRNA. Time-course dependent changes in *Sgk1* mRNA levels in oligodendrocyte primary cultures analyzed after dexamethasone (DEX) administration. Results are expressed as the mean ± SEM of three independent experiments. *p < 0.05, Student's *t*-test. (B) Time-course dependent changes of *Dsg1c* mRNA levels in oligodendrocyte primary cultures analyzed after DEX administration. Results are expressed as the mean ± SEM of three independent experiments. *p < 0.05, Student's *t*-test.

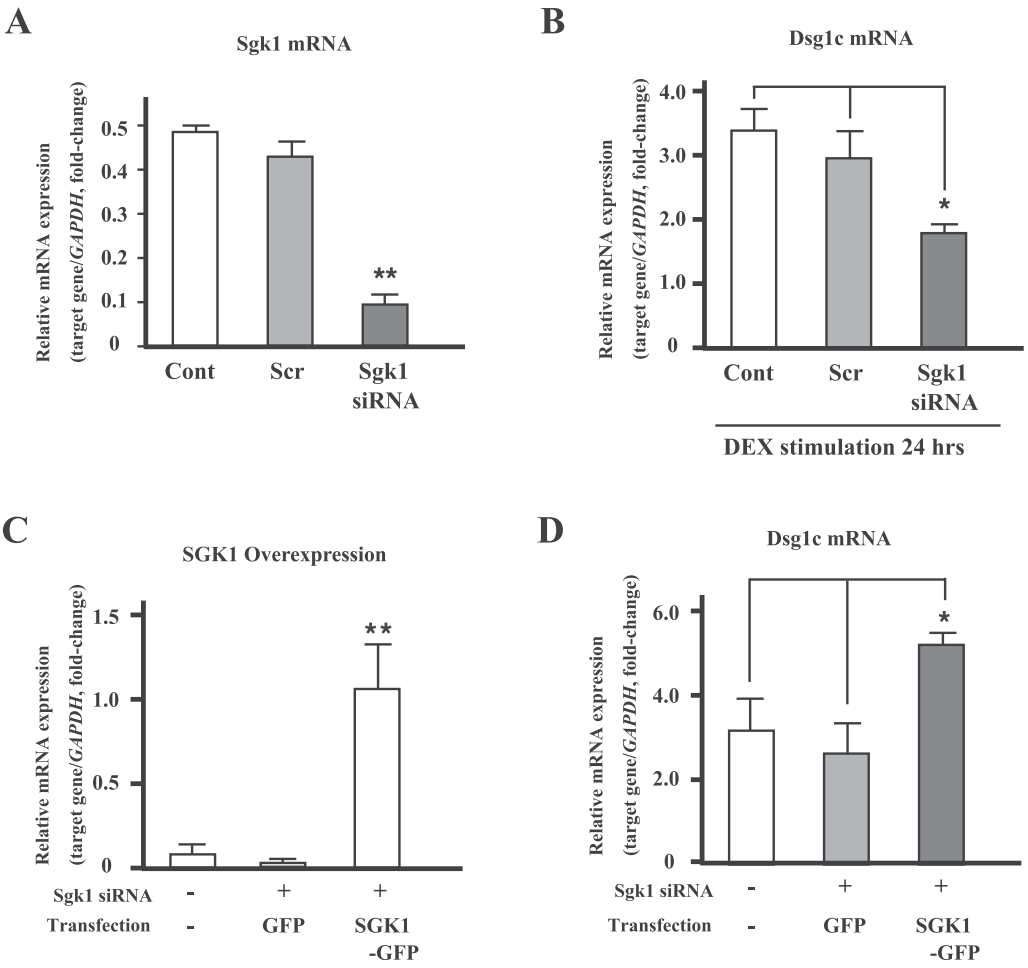

Fig. 4. Sgk1 regulates *Dsg1c* mRNA expression after chronic stress exposure. (A) Real-time PCR analysis of rat *Sgk1* mRNA expression in primary cultures of oligodendrocytes. Cont, non-transfected control; Scr, scrambled siRNA transfection; *Sgk1* siRNA, *Sgk1* siRNA transfection. Results are expressed as the mean ± SEM of three independent experiments. **p < 0.01, Student's *t*-test. (B) Real-time PCR analysis of *Dsg1c* mRNA expression in primary cultures of oligodendrocytes after 24 h of dexamethasone (DEX) exposure. Results are expressed as the mean ± SEM of three independent experiments. *p < 0.05, Student's *t*-test. (C) Real-time PCR analysis of human *SGK1* mRNA expression in primary cultures of oligodendrocytes. GFP, GFP control construct transfection; SGK1-GFP, *GFP*-fused human *SGK1* construct transfection. Results are expressed as the mean ± SEM of three independent experiments. **p < 0.01, Student's *t*-test. (D) Real-time PCR analysis of *Dsg1c* mRNA expression in primary cultures of oligodendrocytes after transfection of *GFP* control (GFP) or *GFP*-fused human *SGK1* constructs (SGK1-GFP). Results are expressed as the mean ± SEM of three independent experiments. *p < 0.05, Student's *t*-test.

Dsp mRNA, could not be detected in the corpus callosum (Fig. 1), it seemed unlikely that Dsg1c forms desmosomes in the corpus callosum. In fact, our electron microscopic analysis failed to detect desmosome-like structures, e.g., keratin intermediate filaments, within the inner dense plaque in the corpus callosum (Fig. 2). Therefore, it is likely that these molecules are involved in a weak connection between the outer and inner surface of the oligodendrocyte, or between the axonal membrane and inner surface of oligodendrocytes.

Previously, we have shown that increased SGK1 expression is induced in oligodendrocytes by the elevation of plasma corticosterone levels caused by repeated exposure to WIRS [7–9]. The present study revealed that upregulation of *Dsg1c* in oligodendrocytes after repeated exposure to WIRS depends on increased *Sgk1* expression, because DEX stimulation of oligodendrocytes caused upregulation of *Dsg1c* expression, while reduction of *Sgk1* expression inhibited this phenomenon (Fig. 4). Our previous studies showed that exposure to chronic stress induce Sgk1 protein phosphorylation and activation in oligodendrocytes; thus, active Sgk1 may be able to regulate *Dsg1c* mRNA expression levels in oligodendrocytes [7,9].

Dsg1 belongs to the desmosomal cadherin family, and is expressed in epidermal keratinocytes as a calcium-dependent cell adhesion molecule [10–12]. This calcium-dependency is well established among classical cadherins and desmosomal proteins [18–21]. Homophilic binding between Dsg1 molecules is affected by the extracellular calcium concentration [22,23]. Therefore, the difference between calcium concentrations at the outer and inner surface of oligodendrocytes, or the axonal membrane and the inner surface of oligodendrocytes in the corpus callosum after repeated exposure to WIRS is of interest.

Dsg1 is involved in activation of p38 mitogen-activated protein kinase (MAPK) and Rho A GTPase [24–26]. It is well known that Rho GTPase signaling and calcium are important cell adhesion regulators in the brain [27–29]. Furthermore, a recent study has indicated that Rho GTPase-related pathways in oligodendrocytes and neurons are involved in antidepressant effects in the hippocampus [30]. Our study suggests that Dsg1 upregulation in oligodendrocytes may be associated with the pathogenesis of major depression following exposure to chronic stress, and implicates morphological regulation of oligodendrocytes by Dsg1-Rho GTPase cascades as a possible mechanism. However, the mechanisms underlying Sgk1-mediated *Dsg1c* regulation in oligodendrocytes are largely unknown; thus, it is important to identify the functions of DSG1 that allow protection against stressful events.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgments

We thank Drs. K. Yamada, T. Takeda, T. Katayama, and Y. Shigeyoshi for their valuable comments. We thank A. Matsumura, A. Kawakami, E. Hisamatsu for their technical assistance. This work was supported in part by the Japan Society for the Promotion of Science, a Grant-in-Aid for Scientific Research on Innovative Areas (grant 26117519), a Grant-in-Aid for Scientific Research (C) (grant 25430079), and the Sakamoto Research Foundation of Psychiatric Diseases.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.bbrc.2015.05.109.

Transparency document

Transparency document related to this article can be found online at http://dx.doi.org/10.1016/j.bbrc.2015.05.109.

References

[1] M. Fava, K.G. Davidson, Definition and epidemiology of treatment-resistant depression, Psychiatr. Clin. N. Am. 19 (1996) 179–200.
[2] R.C. Kessler, P. Berglund, O. Demler, R. Jin, D. Koretz, K.R. Merikangas, A.J. Rush, E.E. Walters, P.S. Wang, The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R), J. Am. Med. Assoc. 289 (2003) 3095–3105.
[3] P.E. Greenberg, R.C. Kessler, H.G. Birnbaum, S.A. Leong, S.W. Lowe, P.A. Berglund, P.K. Corey-Lisle, The economic burden of depression in the United States: how did it change between 1990 and 2000? J. Clin. Psychiatry 64 (2003) 1465–1475.
[4] J.G. Hunsberger, S.S. Newton, A.H. Bennett, C.H. Duman, D.S. Russell, S.R. Salton, R.S. Duman, Antidepressant actions of the exercise-regulated gene VGF, Nat. Med. 13 (2007) 1476–1482.
[5] A. Schmitt, B. Malchow, A. Hasan, P. Falkai, The impact of environmental factors in severe psychiatric disorders, Front. Neurosci. 8 (2011) 19.
[6] E.C. Dunn, R.C. Brown, Y. Dai, J. Rosand, N.R. Nugent, A.B. Amstadter, J.W. Smoller, Genetic determinants of depression: recent findings and future directions, Harv. Rev. Psychiatry 23 (2015) 1–18.
[7] S. Miyata, T. Hattori, S. Shimizu, A. Ito, M. Tohyama, Disturbance of oligodendrocyte function plays a key role in the pathogenesis of schizophrenia and major depressive disorder, Biomed. Res. Int. 2015 (2015) 492367.
[8] M. Tohyama, S. Miyata, T. Hattori, S. Shimizu, S. Matsuzaki, Molecular basis of major psychiatric diseases such as schizophrenia and depression, Anat. Sci. Int. 90 (2015) 137–143.
[9] S. Miyata, Y. Koyama, K. Takemoto, K. Yoshikawa, T. Ishikawa, M. Taniguchi, K. Inoue, M. Aoki, O. Hori, T. Katayama, M. Tohyama, Plasma corticosterone activates SGK1 and induces morphological changes in oligodendrocytes in corpus callosum, PLoS One 6 (2011) e19859.
[10] J. Waschke, The desmosome and pemphigus, Histochem. Cell Biol. 130 (2008) 21–54.
[11] S. Getsios, C.L. Simpson, S. Kojima, R. Harmon, L.J. Sheu, R.L. Dusek, M. Cornwell, K.J. Green, Desmoglein 1-dependent suppression of EGFR signaling promotes epidermal differentiation and morphogenesis, J. Cell Biol. 185 (2009) 1243–1258.
[12] E. Delva, D.K. Tucker, A.P. Kowalczyk, The desmosome, Cold Spring Harb. Perspect. Biol. 1 (2009) a002543.
[13] D. Garrod, M. Chidgey, Desmosome structure, composition and function, Biochim. Biophys. Acta 1778 (2008) 572–587.
[14] S. Shimizu, Y. Koyama, T. Hattori, T. Tachibana, T. Yoshimi, H. Emoto, Y. Matsumoto, S. Miyata, T. Katayama, A. Ito, M. Tohyama, DBZ, a CNS-specific DISC1 binding protein, positively regulates oligodendrocyte differentiation, Glia 62 (2014) 709–724.
[15] K. Yamada, S. Matsuzaki, T. Hattori, R. Kuwahara, M. Taniguchi, H. Hashimoto, N. Shintani, A. Baba, N. Kumamoto, K. Yamada, T. Yoshikawa, T. Katayama, M. Tohyama, Increased stathmin1 expression in the dentate gyrus of mice causes abnormal axonal arborizations, PLoS One 6 (2010) e8596.
[16] Y. Chen, V. Balasubramaniyan, J. Peng, E.C. Hurlock, M. Tallquist, J. Li, Q.R. Lu, Isolation and culture of rat and mouse oligodendrocyte precursor cells, Nat. Protoc. 2 (2007) 1044–1051.
[17] M.W. Pfaffl, I.G. Lange, A. Daxenberger, H.H. Meyer, Tissue-specific expression pattern of estrogen receptors (ER): quantification of ER alpha and ER beta mRNA with real-time RT-PCR, APMIS 109 (2001) 345–355.
[18] N.A. Chitaev, S.M. Troyanovsky, Direct Ca2+-dependent heterophilic interaction between desmosomal cadherins, desmoglein and desmocollin, contributes to cell–cell adhesion, J. Cell Biol. 138 (1997) 193–201.
[19] W. Heupel, D. Drenckhahn, D. Zillikens, J. Waschke, Steric hindrance of desmoglein 3 transinteraction by pemphigus vulgaris IgG, J. Invest. Dermatol. 127 (Suppl. 1) (2007) 5.
[20] O. Pertz, D. Bozic, A.W. Koch, C. Fauser, A. Brancaccio, J. Engel, A new crystal structure, Ca2+ dependence and mutational analysis reveal molecular details of E-cadherin homoassociation, EMBO J. 18 (1999) 1738–1747.
[21] J. Waschke, C. Menendez-Castro, P. Bruggeman, R. Koob, M. Amagai, H.J. Gruber, D. Drenckhahn, W. Baumgartner, Imaging and force spectroscopy on desmoglein 1 using atomic force microscopy reveal multivalent Ca(2+)-dependent, low-affinity trans-interaction, J. Membr. Biol. 216 (2007) 83–92.
[22] P. Elias, S. Ahn, B. Brown, D. Crumrine, K.R. Feingold, Origin of the epidermal calcium gradient: regulation by barrier status and role of active vs. passive mechanisms, J. Invest. Dermatol. 119 (2002) 1269–1274.
[23] G.K. Menon, P.M. Elias, Ultrastructural localization of calcium in psoriatic and normal human epidermis, Arch. Dermatol. 127 (1991) 57–63.
[24] P. Berkowitz, P. Hu, Z. Liu, L.A. Diaz, J.J. Enghild, M.P. Chua, D.S. Rubenstein, Desmosome signaling. Inhibition of p38MAPK prevents pemphigus vulgaris IgG-induced cytoskeleton reorganization, J. Biol. Chem. 280 (2005) 23778–23784.

[25] A.I. Chernyavsky, J. Arredondo, Y. Kitajima, M. Sato-Nagai, S.A. Grando, Desmoglein versus non-desmoglein signaling in pemphigus acantholysis: characterization of novel signaling pathways downstream of pemphigus vulgaris antigens, J. Biol. Chem. 282 (2007) 13804–13812.
[26] J. Waschke, V. Spindler, P. Bruggeman, D. Zillikens, G. Schmidt, D. Drenckhahn, Inhibition of Rho A activity causes pemphigus skin blistering, J. Cell Biol. 175 (2006) 721–727.
[27] T. Saneyoshi, Y. Hayashi, The Ca2+ and Rho GTPase signaling pathways underlying activity-dependent actin remodeling at dendritic spines, Cytoskeleton 69 (2002) 545–554.
[28] E.E. Govek, M.E. Hatten, L. Van Aelst, The role of Rho GTPase proteins in CNS neuronal migration, Dev. Neurobiol. 71 (2011) 528–553.
[29] A. Hall, G. Lalli, Rho and Ras GTPases in axon growth, guidance, and branching, Cold Spring Harb. Perspect. Biol. 2 (2010) a001818.
[30] P. Patrício, A. Mateus-Pinheiro, M. Irmler, N.D. Alves, A.R. Machado-Santos, M. Morais, J.S. Correia, M. Korostynski, M. Piechota, R. Stoffel, J. Beckers, J.M. Bessa, O.F. Almeida, N. Sousa, L. Pinto, Differential and converging molecular mechanisms of antidepressants' action in the hippocampal dentate gyrus, Neuropsychopharmacology 40 (2015) 338–349.