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RESEARCH ARTICLE

Impact of frequency of internet use on development of brain structures and verbal intelligence: Longitudinal analyses

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Abstract

Excessive internet use is shown to be cross sectionally associated with lower cognitive functioning and reduced volume of several brain areas. However, the effects of daily internet use on the development of verbal intelligence and brain structures have not been investigated. Here, we cross sectionally examined the effects of the frequency of internet use on regional gray/white matter volume (rGMV/rWMV) and verbal intelligence as well as their longitudinal changes after 3.0 ± 0.3 (standard deviation) years in a large sample of children recruited from the general population (mean age, 11.2 ± 3.1 years; range, 5.7–18.4 years). Although there were no significant associations in cross sectional analyses, a higher frequency of internet use was found to be associated with decrease of verbal intelligence and smaller increase in rGMV and rWMV of widespread brain areas after a few years in longitudinal analyses. These areas involve areas related to language processing, attention and executive functions, emotion, and reward. In conclusion, frequent internet use is directly or indirectly associated with decrease of verbal intelligence and development to smaller gray matter volume at later stages.

KEYWORDS

brain development, gray matter volume, internet use, verbal intelligence, white matter volume

1 | INTRODUCTION

In the modern age, children spend a significant amount of time on the internet (Jackson et al., 2006). Thus, the impact of this daily habit of children has become the focus of many studies, mainly cross-sectional ones.

Studies on the internet have been conducted in diverse fields, as the contents of internet activity can vary, reflecting the diverse information available online. The internet can be a useful learning tool. For example, internet-based intervention proved to be a useful learning tool for health professions in a meta-analysis (Cook et al., 2008). One focus of studies related to the internet is devices. Mobile phones are widely available in modern times, and long periods of time are spent for internet-based activity. The total time spent using mobile phones was significantly associated with poor sleep habits, declines in study habits, increases in class absence, and increased tardiness for classes in a prior analysis (Gupta, Garg, & Arora, 2016). In addition, increased smartphone use is associated with a less analytic cognitive style and lower cognitive abilities (Barr, Pennycook, Stolz, & Fugelsang, 2015). Smartphone addiction has become increasingly prevalent, and it is associated with perceived stress and poorer academic performance (Samaha & Hawi, 2016). Another focus of studies related to internet is content. For example, internet pornography consumption is one research target, and studies have identified associations of internet pornography consumption with sexual permissiveness (Lo & Wei, 2005). Additionally, internet pornography consumption represents a substantial portion of all pornography consumption, which is associated with brain reward networks (Kühn & Gallinat, 2014). Another popular use of the internet in modern times is social networking. Previous research reported that longer Facebook use is associated with social connectedness (Alloway, Horton, Alloway, & Dawson, 2013), social trust, and life satisfaction (Valenzuela, Park, & Kee, 2009), although social network addiction is associated with greater difficulties with emotion regulation (Hormes, Kearns, & Timko, 2014). Some studies have focused on the use of media including the internet. Studies have illustrated that people who frequently engage in multitasking involving media (primarily driven by internet use) perform worse on cognitive control tasks and exhibit greater socio-emotional difficulties and reduced gray matter density in regions related to attention (Loh & Kanai, 2016).

Contrarily, a substantial number of studies have been devoted to overall internet use, which is the target of the present investigation or overall internet addiction (addictive internet use). Similar to watching television (Kostyrka-Allchorne, Cooper, & Simpson, 2017), internet use has content-specific and overall effects. A high amount of internet use has been shown to be associated with lower school performance in a large sample (Englander, Terregrossa, & Wang, 2010; Kim & So, 2012). In addition, internet addiction which is supposed to accompany greater internet use has been shown to be associated with lower comprehension ability (Park et al., 2011), executive function and impulsivity (Zhou, Zhu, Li, & Wang, 2014), reduced attention, and mood (Bavelier et al., 2011). Also, higher amount of internet use was shown to be longitudinally associated with increase in depression and loneliness (Kraut et al., 1998).

Previous neuroimaging studies have investigated the functional activation related to internet activity and the neural characteristics of individuals with internet addiction (addictive internet use). A functional imaging study has shown that internet searching is associated with higher brain activation in the right orbitofrontal cortex, which is related to reward, and lower brain activation in the right middle temporal gyrus, which is related to language processing (Dong & Potenza, 2015). In addition, internet searching has been shown to be associated with lower accuracy when recalling information (Dong & Potenza, 2015). Conversely, multiple anatomical studies of internet addiction (addictive internet use) (Pezoa-Jares, Espinoza-Luna, & Medina, 2012) have shown a decrease in the regional gray matter volume (rGMV) of the bilateral dorsolateral prefrontal cortex, anterior cingulate, and supplementary motor area, which are involved in executive control and attention (Kondo, Osaka, & Osaka, 2004); the insula, which is involved in emotion processing (Bora, Fornito, Yücel, & Pantelis, 2010); temporal areas, which are involved in language processing (Cabeza & Nyberg, 2000); orbitofrontal areas, which are involved in reward processing (Kringelbach, 2005); and occipital and posterior cingulate areas.

However, these cross-sectional studies cannot strongly address causality, and intervention studies designed to investigate the negative impact of long-term daily habits are practically and ethically difficult. As described above, although the negative impact of higher amount of internet use or internet addiction (addictive internet use) in the youth has been documented, the youth is increasingly spending more time on the internet (Livingstone, 2003). Thus, revealing the longitudinal effects of internet use on the neural systems and intellectual abilities of children is socially and scientifically important.

Based on the aforementioned previous studies, we hypothesized that frequent internet use in children is longitudinally associated with a decline in verbal intelligence (e.g., verbal skills and attentional ability) (Wechsler, 1997) and a reduction (or smaller developmental increase) in the volume of the aforementioned widespread brain areas, including a wide range of prefrontal areas, the anterior cingulate, the insula, and temporal and occipital areas.

The aim of the present study was to test these hypotheses and reveal the effects of internet use via cross-sectional and longitudinal analyses of brain structures and verbal intelligence in children. For this purpose, we performed cross-sectional analyses to identify associations between the frequency of internet use and rGMV/regional white matter volume (rWMV). Using a longitudinal design, we analyzed the associations between the frequency of internet use and changes in rGMV, rWMV, and verbal intelligence after a few years. We evaluated rGMV and rWMV using voxel-based morphometry (Good et al., 2001).

2 | METHODS

2.1 | Subjects

All subjects were Japanese children recruited from the general population. For full descriptions, see Supplemental Methods. The following descriptions have been largely reproduced (have been rewritten in the exact same way in this manuscript) from our previous study of the same project (Takeuchi et al., 2016). As per the Declaration of Helsinki (1991), written informed consent was obtained from each subject and his/her parent. Approval for these experiments was obtained from the Institutional Review Board of Tohoku University. A few years (for details about this interval, see Table 1) after the pre-experiment, post-experiment was conducted and part of the subjects from the pre-experiment also participated in this post-experiment.

Cross-sectional imaging analyses were performed in 284 subjects (138 boys and 146 girls; mean age, 11.2 ± 3.1 years; range, 5.7–18.4 years) and longitudinal imaging analyses were performed in 223 subjects (115 boys and 108 girls; mean age, 14.2 ± 3.0 years; range, 8.4–21.3 years). The socioeconomic background of subjects' families is provided

TABLE 1 Psychological variables of the study participants (mean ± *SD*, range) in the cross-sectional imaging analyses (138 boys and 146 girls, upper lines) and their change in the longitudinal imaging analyses (115 boys and 108 girls, lower lines when there are two lines)

Measure	Boys	Girls
Age (years) (mean ± *SD*, range)	10.9 ± 2.8, 5.7–16.6	11.5 ± 3.3, 5.8–18.4
	3.0 ± 0.3, 1.7–4.0	3.0 ± 0.3, 1.8–4.1
FSIQ (mean ± *SD*, range)	104.1 ± 12.9, 77–134	101.4 ± 11.1, 71–128
	0.5 ± 9.0, −23–24	1.9 ± 9.4, −44–26
VIQ (mean ± *SD*, range)	105.4 ± 13.3, 72–152	102.2 ± 13.0, 67–134
	−0.5 ± 10.3, −28–27	1.4 ± 10.3, −41–22
PIQ (mean ± *SD*, range)	101.7 ± 13.7, 62–136	99.9 ± 11.1, 73–129
	1.6 ± 9.7, −23–26	2.2 ± 10.8, −50–32
Family annual income[a]	4.07 ± 1.49, 1–7	3.86 ± 1.48, 1–7
Average number of years of parents' highest educational qualification	14.4 ± 1.73, 9–18.5	14.1 ± 1.53, 10.5–18.5
Internet use (frequency)[b]	4.79 ± 1.82, 1–7	4.45 ± 1.95, 1–7

[a] Family annual income was classified as follows: 1, annual income below 2 million yen; 2, 2–4 million yen; 3, 4–6 million yen; 4, 6–8 million yen; 5, 8–10 million yen; 6, 10–12 million yen; 7, >12 million yen.

[b] The answer choices consisted of seven options: 1, prohibited (not given); 2, not at all; 3, on rare occasions; 4, 1 day in a week; 5, 2–3 days in a week; 6, 4–5 days in a week; and 7, almost daily.

in Table 1. Furthermore, all the subjects have been students since the start of mandatory education.

No other study is using the data of internet in this cohort.

2.2 | Assessments of psychological variables

The following descriptions, except those of internet use, have been largely reproduced from our previous study of the same project (Takeuchi et al., 2015a). In both pre and post-experiments, we measured the Full Scale intelligence quotient (IQ) using the Japanese version of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) for subjects aged 16 years or older or the Wechsler Intelligence Scale for Children-Third Edition (WISC-III) for subjects younger than 16 years (Azuma et al., 1998). The tests were administered by trained examiners (Fujita, Maekawa, Dairoku, & Yamanaka, 2006). We calculated the Full Scale IQ, verbal IQ (VIQ), and performance IQ (PIQ) for each subject from their WAIS/WISC scores.

In the pre-experiment, information on current internet use habits was collected using a self-report questionnaire with multiple choice questions. The answers to the questions included the following seven options: 1, prohibited (not given); 2, not at all; 3, on rare occasions; 4, 1 day in a week; 5, 2–3 days in a week; 6, 4–5 days in a week; and 7, almost daily. Option 1 means children were not allowed to use the internet (or the technical equipment for internet was not given) by their parents. The values 1–7 were used in subsequent regression analyses. The main analyses separated Options 1 and 2, because the question itself made a distinction between the two as there could be a difference between "prohibited" and "does not choose to do." But even when Option 1 for this question was changed to Option 2, the significance of the analysis results did not change much and the results remained significant. Refer to Supporting Information Methods for the rationale for using this method to evaluate how much one use the internet. We chose to use the measure of frequency of internet use instead of hours of internet use. This is because the previous study already showed the frequency instead of the hours of internet use far more strongly associated with psychological problems among children (Johansson & Götestam, 2004). We only assessed and had the internet use habits at the pre-experiment because this project is a prospective longitudinal cohort study. As described previously (Takeuchi et al., 2015a), to indicate causality at certain levels with analyses in a prospective longitudinal cohort study, it is important that certain variables measured in the pre-experiment period predict (or precede) subsequent changes in other variables. It is a gold standard procedure for prospective longitudinal studies.

Further, as additional covariates, we gathered the following information: number of parents who live together with children, family's annual income, educational qualifications of both parents, and urbanicity (how many people live in the city) of the place (at the municipal level) where the subjects lived, and sleeping hours. For details about these measures, including the detailed methods of assessment, and who answers the questionnaires (guardian or subjects) and its rationale, please see our previous study (Takeuchi et al., 2015a; Taki et al., 2011). Among the covariates, urbanicity of the area of residence (at the municipal level) and sleep duration are not used in many studies in this field (rationale is provided in the Supporting Information Methods). Excluding these two covariates did not alter the significance of the longitudinal imaging analysis findings. However, the results of longitudinal psychological analysis changed from significant to slightly outside the statistical significance level but these subtle changes did not alter our discussion and conclusion (for details, see Supporting Information Methods and Results).

2.3 | Behavioral data analysis

Behavioral data were analyzed using predictive analysis software release version 22.0.0 (PASW Statistics 22; SPSS, Inc., Chicago, IL; 2010). The following descriptions have been largely reproduced from our previous study of the same project (Takeuchi et al., 2016). Multiple regression analyses were used to investigate the associations between internet use and VIQ in the pre-experiment as well as those between internet use in the pre-experiment and the pretest to posttest change in VIQ. In the cross-sectional analyses, sex, age (days after birth), family's annual income, average number of years for parents' highest educational qualification, person who answered the question regarding the internet use, urbanicity of the area in which the participant lived, and sleeping hours as covariates. Additionally, in longitudinal analyses, the time interval between the pre and post-experiment and the independent variable of the cross-sectional analysis (VIQ) were added as covariates. Although the primary outcome measure in this behavioral analysis was the effect of internet use on VIQ, other IQ test scores were investigated in the same manner. The rationale of inclusion of urbanicity of the area, sleeping hours as covariates is due to their effects on neural and cognitive systems (Lederbogen et al., 2011; Taki et al., 2011) as well as it is likely these variables are associated with internet use.

2.4 | Image acquisition

All images were collected using a 3-T Philips Intera Achieva scanner. Three-dimensional, high-resolution, T1-weighted images (T1WI) were collected using a magnetization-prepared rapid gradient-echo sequence. The parameters were as follows: 240 × 240 matrix, TR = 6.5 ms, TE = 3 ms, TI = 711 ms, FOV = 24 cm, 162 slices, 1.0-mm slice thickness, and scan duration of 8 min and 3 s.

2.5 | Preprocessing and analysis of structural data

Pre-processing of the structural data was performed using Statistical Parametric Mapping software (SPM12; Wellcome Department of Cognitive Neurology, London, UK) implemented in MATLAB (Mathworks, Inc., Natick, MA). For cross-sectional analyses of the images, using the new segmentation algorithm implemented in SPM12, T1-weighted structural images of each individual were segmented and normalized to the Montreal Neurological Institute (MNI) space to give images with 1.5 × 1.5 × 1.5 mm^3 voxels using diffeomorphic anatomical registration through exponentiated lie algebra (DARTEL) registration process implemented in SPM12. In addition, we performed a volume change correction (modulation) (Ashburner & Friston, 2000). Subsequently, generated rGMV and rWMV images were smoothed by convolving them with an isotropic Gaussian kernel of 8 mm full width at half maximum (FWHM). For full descriptions of these procedures, see Supporting Information Methods.

For longitudinal analyses, the pairwise Longitudinal Registration toolbox (Ashburner & Ridgway, 2013) and new segmentation algorithm implemented in SPM12 were used to register the pre and post-experiment T1WIs, and maps of changes in rGMV and rWMV were calculated. In addition, using DARTEL procedures normalized to the MNI space, images with 1.5 × 1.5 × 1.5 mm^3 voxels were obtained. Subsequently, the generated maps of changes in rGMV and rWMV were smoothed by convolution with an isotropic Gaussian kernel of 8 mm FWHM. For full descriptions of these procedures, refer to Supporting Information Methods.

2.6 | Statistical analysis

Statistical analyses of imaging data were performed with SPM8.

In cross-sectional whole-brain multiple regression analysis of the main effect of internet use, we included only voxels with an rGMV (or WMV) signal intensity of >0.05. Cross-sectional whole-brain multiple regression analysis was performed to investigate the association between rGMV or rWMV and internet use. The covariates were the same as those used in the psychological cross-sectional analyses except that in imaging analyses, the total intracranial volume (TIV) calculated using voxel-based morphometry (for details of calculation see the reference Takeuchi et al., 2015b) was added as a covariate.

In longitudinal whole-brain multiple regression analysis of the main effect of internet use, the analysis was limited to areas where the average rGMV value for the segmented and normalized mean images of prescans and postscans of all participants was greater than 0.05. In longitudinal analyses of rGMV (or rWMV), we determined the associations between internet use and maps representing the signal changes in rGMV (or rWMV) between the pre and post-experiment images (meaning dependent variable at each voxel was signal of the map of the change of rGMV (or rWMV). The covariates were the same as those used in the psychological longitudinal analyses except that in imaging analyses, TIV in the pre-experiment was added as a covariate.

A multiple comparison correction was performed using threshold-free cluster enhancement (TFCE) (Smith & Nichols, 2009) with randomized (5,000 permutations) nonparametric testing using the TFCE toolbox (http://dbm.neuro.uni-jena.de/tfce/). We applied a threshold of family-wise error corrected at $p < .05$.

SPM8 was used here because of better compatibility of the software of TFCE and home-made script for analyses. As long as TFCE is used, the rationale for estimating the statistical significance is same, and this would not matter to the results.

3 | RESULTS

3.1 | Basic data

The characteristics of the subjects are shown in Table 1. Intelligence of subjects showed a normal value. The distribution of frequency of internet use for all the subjects, which was collected by a self-report questionnaire, is shown in Figure 1. Majority of subjects do not rarely use internet or do not use internet in the daily life.

The studies in this project including the present study included subjects with IQ < 80. The rationale for using this criterion and the effects of excluding this criterion are provided in the Supporting Information Methods and Results.

3.2 | Cross-sectional behavioral analysis

After correcting for confounding variables, multiple regression analysis using pre-experiment data revealed that the frequency of internet use in the pre-experiment did not significantly correlate with VIQ in the pre-experiment [$p = .150$, standardized partial regression coefficient

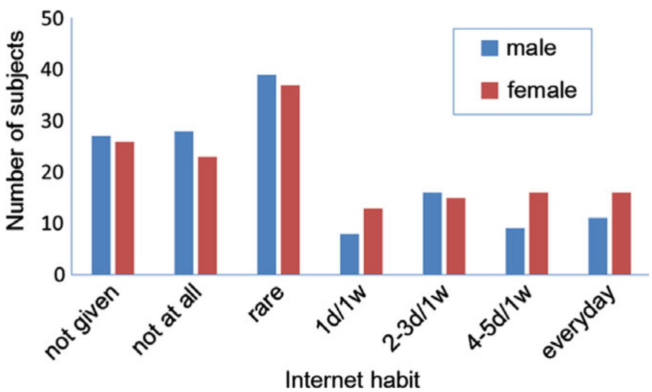

FIGURE 1 Histograms showing the internet use (frequency) of boys and girls in the sample

(β) = 0.097, t = 1.443]. We subsequently investigated the association of frequency of internet use with FSIQ and PIQ; however, the frequency of internet use did not significantly correlate with FSIQ in the pre-experiment (p = .626, β = 0.033, t = 0.487) and PIQ in the pre-experiment (p = .439, β = −0.052, t = −0.775).

3.3 | Longitudinal behavioral analysis

After correcting for confounding variables, multiple regression analysis performed using longitudinal data revealed that the frequencies of internet use in the pre-experiment were significantly and negatively correlated with the VIQ change between the pre and post-experiment data (p = .034, β = −0.151, t = −2.129, Figure 2). We subsequently investigated the association of the frequency of internet use with changes in FSIQ and PIQ. The frequency of internet use showed a significant negative correlation with the FSIQ change between the pre and post-experiment data (p = .043, β = −0.144, t = 2.033) but not with the PIQ change between the pre and post-experiment data (p = .194, β = −0.091, t = −1.30).

3.4 | Cross-sectional rGMV/rWMV analysis

After correcting for confounding variables, multiple regression analysis using pre-experiment data revealed that the frequency of internet use did not significantly correlate with rGMV or rWMV of any of the brain areas.

3.5 | Longitudinal rGMV/rWMV analysis

After correcting for confounding variables, whole-brain multiple regression analysis performed using longitudinal data revealed that the frequency of internet use in the pre-experiment showed a significant negative correlation with the change in rGMV of a widespread anatomical cluster, particularly including extensive bilateral perisylvian areas, the bilateral temporal pole, the bilateral cerebellum, bilateral medial temporal lobe structures (hippocampus and amygdala), bilateral basal ganglia structures, the bilateral inferior temporal lobe, the thalamus, the bilateral orbitofrontal gyrus and lateral prefrontal cortex, the insula, and the left lingual gyrus (Figure 3a,b and Supporting Information Table S1).

After correcting for confounding variables, whole-brain multiple regression analysis performed using longitudinal data revealed that the frequency of internet use in the pre-experiment showed a significant negative correlation with the change in rWMV of a widespread anatomical cluster that spread to the WM area adjacent to the aforementioned rGMV cluster and cingulate areas (Figure 4a,b and Supporting Information Table 2).

4 | DISCUSSION

As described in Section 1, previous cross-sectional studies have reported that negative psychological and neural characteristics are associated with internet addiction (addictive internet use). In the present study, we revealed the novel effects of the frequency of internet use in children recruited from the general population via cross-sectional and longitudinal analyses. Our hypotheses were partly

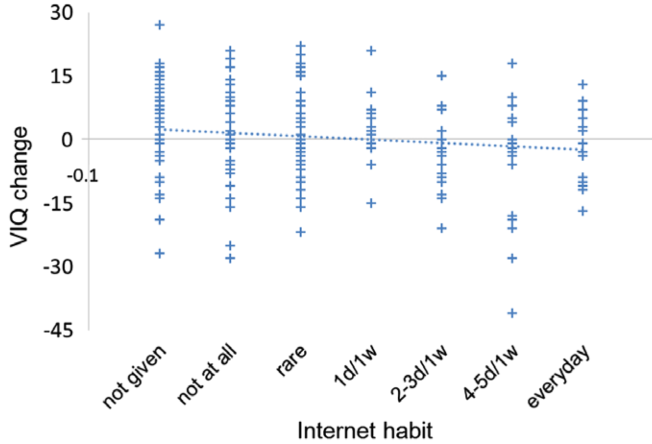

FIGURE 2 The association between internet use (frequency) and VIQ change across time. The scatter plot and accompanying trendline depict the association between internet frequency and longitudinal VIQ change. After correcting for confounding variables, a lower frequency of internet use was significantly associated with an improvement in VIQ from pre to post-experiment

confirmed and although cross sectional differences in the frequency of internet use were not associated with outcome measures, unlike the aforementioned findings in internet addiction (addictive internet use), a higher frequency of internet use was associated with decreased verbal intelligence and smaller volume increases in widespread brain areas after a few years. These brain areas are related to language processing, attention and executive functions, emotion, and reward, as discussed and hypothesized subsequently. The longitudinal correlations could not be caused by age, simply because age is corrected in longitudinal analyses.

The areas that showed a significant decrease in rGMV and rWMV in response to an increase in the frequency of internet use are related to language processing, memory, attention, and executive functions. Among the areas found to be significantly affected in our study, the left perisylvian region is consistently activated during a wide range of language processing and is considered to play a key role in these processes (Cabeza & Nyberg, 2000). The hippocampus, which is involved in memory formation and learning new information, appears to be associated with increased rGMV of this area (Draganski et al., 2006). The lateral prefrontal regions are involved in the manipulation or mental operation of objects retained in one's mind, executive functioning, attention, and working memory (Baddeley, 2003; Owen, 2000). The cerebellum has many functions; however, one of the key functions of this region involves the phonological loop (Baddeley, 2003), which together with perisylvian areas is suggested to be part of the phonological loop of WM that enables verbal information to be stored in WM (Osaka & Nishizaki, 2000). We speculate that the smaller rGMV development in these regions due to frequent internet use may be associated with a decrease in verbal intelligence, which is measured by the Wechsler IQ test and involves verbal skills, knowledge, attention, and working memory (Wechsler, 1997).

From the present findings, we can only speculate the mechanisms underlying these associations. A decrease in neural tissues such as spines based on the mechanisms underlying use-dependent plasticity, which is caused by decreased activities (Takeuchi and Kawashima, 2016) during internet use, may be one such mechanism. For example, hippocampal activity and memory performance have been shown to decrease during internet use (Dong & Potenza, 2015).

The brain areas that showed a significant decrease in rGMV and rWMV in response to increased frequency of internet use also involve emotion and reward. The insula is activated in response to a wide range of cognitive processes (Chang, Yarkoni, Khaw, & Sanfey, 2013); therefore, it is difficult to infer how this region may be affected by internet use based on the present findings. However, as stated in Section 1, this area is critically involved in emotion processing (Chang et al., 2013). In addition, rGMV of the insula is reduced during depression (Bora et al., 2010) and a wide range of psychiatric diseases involving depression (Phillips, Drevets, Rauch, & Lane, 2003). Similarly, areas such as the amygdala are functionally involved in emotional processing, and their volume is reduced during depression (Phillips et al., 2003). Conversely, the orbitofrontal cortex and putamen are known to be part of the reward system and are involved in motivation as well (Naranjo, Tremblay, & Busto, 2001). It is known that internet activity is highly rewarding and the orbitofrontal cortex is activated during internet activity (internet searching) (Dong & Potenza, 2015). Engagement in these types of highly rewarding activities is suggested to lead to desensitization to reward and loss of ability to enjoy pleasure, resulting in depressive mood (Naranjo et al., 2001). Perhaps, through these cascades, structural changes in these regions may be induced. In addition, the regional gray matter structure of the orbitofrotnal cortex is related to impulsivity (Yokoyama et al., 2015); thus, through the changes in these neural mechanisms, frequent internet use may be associated with depressive moods and impulsivity (LaRose, Eastin, & Gregg, 2001; Spada, 2014). However, these statements are highly speculative, and we did not gather information relevant to depression and impulsivity in the present study. Future studies may be needed to ascertain the validity of these speculations.

The present study has advanced our understanding of the direct and indirect effects of frequent internet use in children. As described in Section 1, previous studies have shown lower psychological performance in children with excessive internet use (for details see Section 1). Neuroimaging studies have shown reduction in the volume of brain areas in these subjects as well. In the present study, we longitudinally investigated the effects of the frequency of internet use in children recruited from the general population and have shown frequent internet use is directly or indirectly associated with development to smaller verbal intelligence and smaller gray matter volume in this sample. These data suggest the causality of frequent internet use more strongly than cross-sectional studies.

The reason why we did not observe significant associations in cross-sectional behavioral analysis may be related to the multiple factors that could work to form the positive associations between internet use and behavioral and structural outcome measures, despite the general negative impact of internet use as described below. First, internet use is associated with preferable environments that could facilitate verbal and structural development. For example, a higher socioeconomic status in childhood leads to greater internet use in later life (Silver, 2014) (although associations between the socioeconomic status and frequency of internet use were weak and not significant in the present study). Second, cross-sectional analysis showed that internet use is beneficial for reading skills in children with low reading ability (Jackson, Von Eye, Witt, Zhao, & Fitzgerald, 2011), perhaps indicating that internet use may facilitate primitive language skills initially, but these effects may not last long after the acquisition of such skills (and may not appear in longitudinal analyses). Third, children with greater intelligence may (be able to) use the internet more frequently for various reasons. These factors may erase the negative causal impact of internet use on verbal intelligence in cross-sectional analyses. Future studies are needed to investigate these possibilities. Consistently, when we divided subjects into older and younger groups, there were significant interaction effects between this age group and the frequency of internet use on rWMV of the right parietal areas in cross-sectional analysis (see Supporting Information Figure 1, Methods, and Results for details). A similar tendency was observed in widespread frontal and parietal areas when a more lenient threshold was used (Supporting Information Figure 2). This result was observed by the tendency toward a positive association between the frequency of internet use and rWMV in younger children and the opposite tendency in older children. This finding may be consistent with all the possibilities mentioned in this paragraph, considering that the cumulative effects of long-term internet use in older subjects may erase the positive association between the frequency of internet use and rWMV that may be formed through the mechanisms mentioned in this paragraph. The impact of other possibilities such as the use of the internet for different purposes by older and younger subjects cannot be ruled out, and future studies are needed to confirm which of these possibilities is correct.

Regarding brain areas associated with the significant correlations between internet use and longitudinal rGMV and rWMV changes, although the areas were dispersed bilaterally, only right (but not left) temporoparietal regions were identified as areas of significance (Figures 3 and 4). However, when the threshold was lowered to $p = .10$ and correction was performed, similar trends were observed in the left homolog (Supporting Information Figure 3). Therefore, it is difficult to conclude whether internet use was associated with regional brain volume changes in the left hemisphere or whether the changes are stronger in the right temporoparietal regions. Future studies are needed to investigate this issue with greater statistical power.

Furthermore, it should be noted that the present study investigated the effects of internet use in children and the effects of internet use could vary between different groups. In the elderly, internet use has been shown to be consistently associated with better cognitive functioning and moods (Hamer & Stamatakis, 2014; Tun & Lachman, 2010), and some intervention studies have shown the beneficial effects of interventions using the internet (van der Wardt, Bandelow, & Hogervorst, 2010). Thus, the effects of internet use on the neural mechanisms in other groups should be investigated in future studies.

The present study had some limitations. First, as discussed in our previous study of a similar project (Takeuchi et al., 2015b), this was not an intervention study. Thus, although we have shown a correlation between the frequency of internet use at one point and the longitudinal change in verbal intelligence and brain structures later, we

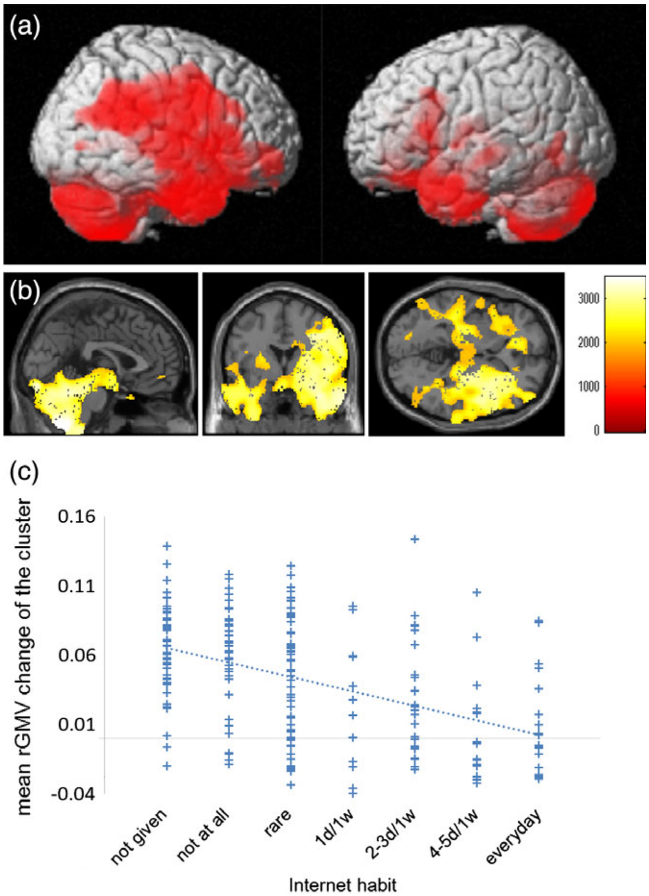

FIGURE 3 The longitudinal association between internet use (frequency) and rGMV change across time. After correcting for confounding covariables, frequent internet use was significantly associated with greater (relative) rGMV increase. (a and b) The results shown were obtained using a threshold of TFCE of $p < .05$, based on 5,000 permutations. The results were corrected at the whole brain level. We observed significant associations with a large anatomical cluster that mainly included perisylvian areas, orbitofrontal and lateral prefrontal areas, the insula, the putamen, the pallidum, the thalamus, medial temporal areas, the anterior temporal pole, and the cerebellum. (a) The results were projected onto the rendered image of SPM8. (b) The regions of correlation are overlaid on an SPM8 "single subject" T1 image. The color bar represents TFCE value. (c) The scatter plot and accompanying trendline depict the association between internet frequency and mean longitudinal change in rGMV of the significant cluster. *Y* axis represents signal intensity of map of rGMV change. Note the results can extend into white matter areas because of smoothing

cannot clarify whether internet use itself directly affects these measures. There is a possibility that a reduction in the number of beneficial activities (e.g., reading, studies, interacting with others, and exercise) due to the increased time spent on the internet may directly affect these measures. In addition, when children sleep for 8 hr and go to school for 8 hr, the time remaining during the day is limited; thus, if they only spend a certain amount of time on specific activities, other activities are naturally compensated, and these all other compensated activities may be important for the observed changes in outcome measures. We believe that even if this is the case, the purpose of our study was fulfilled because we determined that compared with other activities, internet use is not beneficial for the development of verbal intelligence and brain structural development. However, as discussed earlier, there is some evidence to suggest that under certain conditions (children without primitive language skills), internet use may help children to develop primitive language skills. Future studies may be able to investigate this issue more precisely. Alternatively, certain individual tendencies toward internet use may affect brain structures and verbal intelligence. We had corrected potential confounding variables in the multiple regression analyses. And other variables such as the relationship with parents, and personalities related to the developmental disorder (empathizing and systemizing) (Sassa et al., 2012) that were gathered in the pre-experiment of this project did not show significant relationship with frequency of internet ($p > .1$, $|r| < 0.1$). But ultimately, this possibility cannot be ruled out in nonintervention

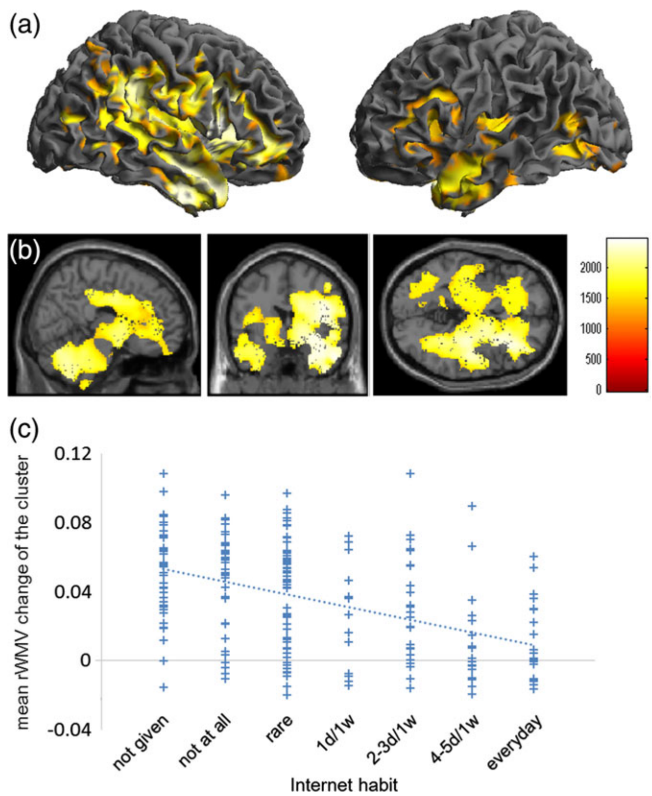

FIGURE 4 The longitudinal association between internet use (frequency) and rWMV change across time. After correcting for confounding covariables, frequent internet use was significantly associated with greater (relative) rWMV increase. (a and b) The results shown were obtained using a threshold of TFCE of $p < .05$, based on 5,000 permutations. The results were corrected at the whole brain level. We observed significant associations with a large anatomical cluster that mainly included the white matter area beneath or near perisylvian areas, orbitofrontal and lateral prefrontal areas, the insula, the putamen, the pallidum, the thalamus, medial temporal areas, the anterior temporal pole, middle and anterior cingulate areas, and the cerebellum. (a) The results were projected onto the surface image of SPM8. (b) The regions of correlation are overlaid on an SPM8 "single subject" T1 image. The color bar represents TFCE value. (c) The scatter plot and accompanying trendline depict the association between internet frequency and mean longitudinal change in rWMV of the significant cluster. *Y* axis represents signal intensity of map of rWMV change. Note the results can extend into CSF areas because of smoothing

longitudinal studies. Future intervention studies may be necessary to completely rule out this possibility. Furthermore, the cohort project including the present study began in 2008, when smartphones were not available and online games were not well-known in Japan. To the best of our knowledge, at present, children may engage in more online activities with the development of these new technologies (Rideout, 2016), and the effects of these new technologies should be investigated in future studies. Further, like most relevant previous studies of internet use and internet addiction or dependency (e.g., Englander et al., 2010; Kim & So, 2012; Kraut et al., 1998), we did not gather information regarding the type of internet use (e.g., email or internet surfing) or purpose (e.g., social network site or studying) because these details were out of the scope of our study, and our study was underpowered to perform these types of subanalyses. The overall amount of internet use was associated with problematic outcomes and work as distractors to children in prior studies (e.g., Englander et al., 2010; Kim & So, 2012; Kraut et al., 1998), and the negative impact of overall internet use appears predominant. However, this does not rule out the positive effects of certain types of internet use, as the internet is a useful source of information. Future studies are needed to investigate these issues. Moreover, in the present study, we did not gather information on internet addiction and did not differentiate between the frequency of normal and addictive internet use. However, we believe that this is not a major issue. Most children did not use the internet seven times a day in the present study, which may indicate that subjects with these characteristics are rare. This may be because internet addiction is typically observed in subjects in their 20s–30s (Shaw & Black, 2008). Our data (Figure 2–4) shows a pattern that children with a moderate level of internet use (1–3 days a week) show a decline in structural and cognitive development of the brain compared with children with a lesser level of internet use (rare, not at all, not given), though this is not a statistically clarified issue. As we discussed earlier (Takeuchi et al., 2016), it is difficult to differentiate between addiction and excessive use statistically in this type of observational study because these factors tend to strongly correlate with one another. These issues may be effectively resolved through a well-designed intervention study.

In conclusion, frequent internet use is directly or indirectly associated with decrease of verbal intelligence and development to smaller gray matter volume at later stages.

A definitive conclusion may require intervention studies, which may be difficult; however, guardians of children should consider these effects when children engage in frequent internet use.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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