Association between visual status and the frequency of laughter in older Japanese individuals: the JAGES cross-sectional study

Akira Inoue,1 Yoshimune Hiratsuka,1 Atsuhide Takesue,2 Jun Aida,3 Katsunori Kondo,4,5 Akira Murakami6

ABSTRACT

Objective Although the beneficial effects of laughter are abundantly reported, the physical function that is required as a premise for laughter has not been studied. The aim of this study is to investigate the association between visual status and frequency of laughter in a population-based sample of older adults.

Methods and analysis We analysed cross-sectional data of community-dwelling independent individuals aged ≥65 years (n=19,452) in Japan. The outcomes were frequency of laughter and number of opportunities to laugh. We used multivariable logistic regression analysis with multiple imputations to investigate the association between visual status and laughter.

Results The number of participants who laughed almost every day was 8,197 (42.1%). After adjusting for individual covariates in the multivariable logistic regression analysis with multiple imputations, visual status was found to be significantly associated with the frequency of laughter and the number of opportunities to laugh (p for trend <0.01). Compare to ‘normal vision’, while excellent/very good vision was associated with increased frequency and number of opportunities to laugh (ORs: 1.72 and 1.25, respectively), poor vision decreased the frequency and number of opportunities to laugh (ORs: 0.86 and 0.87, respectively).

Conclusions There is a link between visual impairment and laughter, with poor vision having a negative impact while good vision has a positive effect. Improving vision may lead to laughter promotion.

INTRODUCTION

Laughter is a universal human behaviour, and every human is genetically predisposed to develop the ability to laugh. Laughter was accorded high evolutionary significance by Charles Darwin (1872), and it is suggested that a primitive precursor to human laughter has evolutionary origins in the common primate ancestor of humans at least 6.5 million years ago.1 Humour and laughter have played an important role in human culture since the beginning of recorded time. The positive effects of humour and laughter are referenced in The Bible, Book of Proverbs 17:22 (NIV): ‘A cheerful heart is good medicine, but a crushed spirit dries up the bones’. This indicates that people in the 10th century already understood the health benefits of humour and laughter.2

Fry was a pioneering investigator who, in the 1960s, coined the term gelotology: the study of laughter. His work provided mechanistic insights and evidence for the positive physiological impact of laughter and humour.3 Various benefits of laughter include alleviation of pain of ankylosing spondylitis,4 allergic skin reaction,5 and radiation dermatitis6; positive effects on the neuroendocrine-immune system7; endogenous opioid release8; and improvement of blood vessel function,9 cardiovascular diseases,10 depression,11 subjective health,12 cancer care management,13 and functional disability.14 The link between laughter and gene expression was also demonstrated using DNA microarray techniques: of 18,716 genes, eight were upregulated and 15 were downregulated after a laughing episode.15 Five of the eight upregulated genes were associated with cell adhesion, apoptosis and cell cycle. The

Key messages

What is already known on this topic?
- The relationship between visual impairment and laughter has not been examined.

What this study adds?
- There is an association between visual impairment and laughter, with poor vision having a negative impact while good vision has a positive effect.

How this study might affect research, practice or policy?
- Improving eyesight may be helpful for laughter-provoking physical and mental benefits and a joyful life that relates to well-being.
beneficial effects of laughter on diabetic nephropathy in terms of normalising the expression of the prorenin receptor gene are strongly suggested. Pain and cortisol levels could be decreased by laughter-inducing therapies, which show promise, especially for depression, although further research is needed to support this conclusion.

Although the brain laughter circuit has been discussed in the field of neurophysiology, and the beneficial effects of laughter are abundantly reported, the physical function that is required as a premise for laughter remains unknown. In fact, from the epidemiological point of view, an obstacle to triggering laughter and the extent of its negative effects on laughter have not been studied. Newborn babies laugh spontaneously as early as 5–9 weeks. The number of situations that elicit laughter, which mainly include tactile, social playing, auditory, and/or visual stimulation, increases with age. In adults, most opportunities to laugh follow visual or auditory stimulation, which is processed in the dorsal upper pons. Thus, we hypothesised that there may be a connection between visual impairment and laughter. Visual impairment could negatively affect laughter, and there is a possibility that those with visual impairment have limited opportunities to laugh in daily life.

The prevalence of visual impairment approximately triples with the progression of each decade of life beyond the age of 40 years and, in developed countries, the prevalence of eye diseases and visual impairment has been increasing, which is driven by population ageing. In Japan, half of the population with visual impairment is older than 70 years, and the number of visually impaired persons is projected to rise in the future. Therefore, we examined the relationship between self-reported visual status and laughter. If visual impairment is shown to have a negative effect on laughter, this would suggest the importance of preventing and treating visual impairment and implementing social support programmes for visually impaired individuals.

METHODS

Data were acquired from the Japan Gerontological Evaluation Study (JAGES), an ongoing prospective cohort study on social determinants of health among functionally independent adults aged ≥65 years. JAGES seeks to understand the social determinants of healthy ageing. Surveys, which are approximately biennial, inquire about health habits, psychological factors and a broad range of social determinants. To date, six waves of questionnaire surveys have been conducted between 2003 and 2019. The survey was a self-administered questionnaire that was returned by postal mail. The questionnaire forms were distributed to participants via the local government. The present study is based on cross-sectional data from the 2016 survey, conducted in 39 municipalities between October 2016 and January 2017. The municipalities include urban/suburban and rural communities from the north (Hokkaido; the northernmost area) and south (Kyushu; the south area) in Japan. These municipalities were not randomly selected as the survey was conducted in collaboration with local municipalities. However, the target population was randomly selected, or, in small municipalities, the entire population was targeted. Of the 279,661 questionnaires distributed, 196,438 (response rate, 70.2%) were completed. The survey questionnaire consisted of core and non-core items. Core items were distributed to all targeted populations. There were eight modules of non-core items, and people randomly received one module with the core items. Wave 2016 contained questions regarding visual status in one module of the non-core items, and 2295 people responded to this questionnaire. In this study, we focused on people living independently. The 2839 participants who answered ‘needs care or assistance in daily life’ or did not respond to this questionnaire were excluded. Among those persons, 19,452 participants, excluding four respondents who did not report their gender were analysed. If respondents experienced difficulty in reading or completing the questionnaire, their family members or friends were allowed to help.

Visual status

Visual status was measured by a self-administrated questionnaire, translated from the English Longitudinal Study of Ageing. To determine self-reported visual status, respondents were asked a single question: is your eyesight (using glasses or corrective lens as usual): excellent; very good; good; fair; or poor? Self-reported visual status has previously demonstrated a significant association with objective visual acuity.

Laughter

We analysed two variables: frequency of laughter and number of opportunities to laugh. The daily frequency of laughter was measured based on the response to the following standard single-item question: ‘How often do you laugh out loud?’ The possible item answers were: almost every day; 1–5 days/week; 1–3 days/month; and <1 day/month. Based on a previous study, we defined participants as laughing if their answer was ‘almost every day’. Regarding the second variable of laughter, respondents were asked to check-up to eight different opportunities for laughing: while having conversations with friends; conversations with a partner; conversations with children and grandchildren; watching TV and videos; listening to the radio; watching comic story tellings and plays; reading comics and magazines; and other. The total number of opportunities for laughter in which each subject participated was tallied. If the number of opportunities were ≥4, it was considered high.

Covariates

We used several covariates on the basis of previous works: age (65–69, 70–74, 75–79, 80–84, and ≥85 years old); sex; marital status (married, widowed, separated, or unmarried); educational attainment (<9 years, 10–12 years, or ≥13 years); equivalised household income (<2
million yen=‘low,’ 2–3.99 million yen=‘middle,’≥4 million yen=‘high’); depressive symptoms, frequency of meeting friends; social participation; and physical health status. For the evaluation of depressive symptoms, the Geriatric Depression Scale–15, a 15-item questionnaire with a score range of 1–15, was used: the higher the scores, the greater the depressive symptomatology. As described in previous studies, we used five as the cut-off score for depression, indicating moderate to severe psychological distress.28 Socioeconomic status and degree of social activities could confound the effect of visual impairment on laughter. The frequency of meeting friends and acquaintances was measured with a question comprising six categories: ≥4 days/week; 2–3 days/week; 1 day/week; 1–3 days/month; several times/year; and none. We divided the respondents into two groups: <2–3 days/week or ≥2–3 days/week. Social participation was defined as involvement in any type of social activity during the study period. Respondents were asked how often they took part in volunteer groups, sports groups, hobby groups, senior citizen clubs, neighbourhood associations, study/cultural groups, health promotion groups, or teaching skills/passing on experiences to others. The frequency of participation was assessed as: ≥4 times/week; 2–3 times/week; once a week; 1–3 times/month; several times/year; or never. We defined ‘social participation’ as participating in a group with a frequency of at least several times per year. To assess the intensity of overall social participation, we generated a total participation score. The total number of types of organisations in which each subject participated was tallied, and participation was categorised as no participation and participation in one, two, and three or more organisations. Physical health status is associated with both laughter and visual status. Respondents were asked whether they had a history of systemic comorbidities, including hypertension, stroke, diabetes, blood and immune diseases, and eye diseases, because these systemic conditions and diseases can cause ocular complications. Subjects were categorised as: no history; one; two; or three or more diseases (multi-morbidity).

Statistical analysis
All study variables were subjected to a descriptive analysis. We performed univariate and multiple logistic regression analyses to calculate the ORs and 95% CIs of frequency of laughter and the number of opportunities of laughing according to visual status. For the frequency of laughing, we dichotomised it into ‘higher frequency of laughing (answered ‘almost every day’ to=1)’ and ‘lower frequency of laughing (answered less than ‘1–5 days/week’ to=0’). For the number of opportunities of laughing, we dichotomised it into ‘higher opportunities of laughing (answered ‘≥4 Opportunities’ to=1)’ and ‘lower opportunities of laughing (answered less than ‘2–3 Opportunities’ to=0’). In the models, to estimate the effects of both excellent and impaired vision status, we used ‘good’ vision as a reference. P for trend was calculated to examine the linear pattern of association of visual status with laughter. We adjusted for the following possible confounding factors: age, sex, marital status, educational attainment, equivalised household income, depressive symptoms, frequency of meeting friends, social participation score and history of systemic comorbidities. Prior to conducting logistic regression analysis, the problem of missing values was addressed using multiple imputations. Under a missing-at-random assumption, we created 10 imputed groups of data using chained equation method, made analyses for each dataset, and combined the 10 results using Rubin’s combination method.29 All variables included in the analyses were used for multiple imputations. Each imputation was based on regression models of the analysed variables. Following the chained equation method, we performed a logistic regression for binary variables (history of systemic comorbidities), a multinomial logistic regression for categorical variables (marital status), and an ordinal logistic regression for ordinal variables (visual status, frequency of laughing, number of opportunities to laugh, years of education, equivalised income, depressive symptoms, frequency of meeting friends and social participation) in multiple imputation. We also conducted univariate and multiple logistic regression analyses with the complete cases without missing data for a sensitivity analysis. We used Stata 15 (StataCorp) for the analyses, and set a significance level at 5%.

Patient and public involvement
No patient or the public was involved in the development of the research question and design of this study. The results of this study will be disseminated to stakeholders such as local and central health governments after being published in a scientific journal.

RESULTS
The mean age ±SD of the participants was 73.7±6.0 years (range, 65–100) years, and 46.1% of participants were men. Table 1 summarises the basic characteristics of individuals according to visual status with multiple imputations. The overall prevalence of laughter (almost every day) (8197 in 19 452 participants) was 42.1% (95% CI 41.4 to 42.8). Individuals with a good visual status tend to laugh more frequently than do those with a poor visual status. Approximately 31% and 56% of those with poor and excellent vision, respectively, reported that they laugh almost every day. On the contrary, approximately 14% and 4% of those with poor and excellent vision, respectively, reported that they laugh <1 day/month. The number of opportunities to laugh was ≥4 (5020 in 19 452 participants) in 25.8% (95% CI 25.2 to 26.4) of participants. Approximately 18% and 32% of those with poor and excellent vision, respectively, reported that the number of opportunities to laugh was ≥4. On the contrary, approximately 34% and 18% of those with poor and excellent vision, respectively, reported that the number of opportunities to laugh was <1.

Table 2 summarises the results of the univariate and multiple logistic regression analysis with multiple
Table 1  Descriptive characteristics of the study participants by visual status with multiple imputation (n=19 452)

| Variables                        | Visual status |
|---------------------------------|---------------|
|                                 | Excellent (n=1770) | Very good (n=5669) | Good (n=10 475) | Fair/poor (n=1539) | Total (n=19 452) |
| Frequency of laughing, n (%)    |               |                  |                  |                    |                  |
| Almost every day                | 990 (55.9)  | 2649 (46.7)  | 4079 (38.9)  | 480 (31.2)  | 8197 (42.1) |
| <1–5 days/week                  | 560 (31.6)  | 2215 (39.1)  | 4294 (41.0)  | 597 (38.8)  | 7666 (39.4) |
| 1–3 days/month                  | 148 (8.3)   | 589 (10.4)   | 1424 (13.6)  | 254 (16.5)  | 2415 (12.4) |
| <1 day/month                    | 73 (4.1)    | 215 (3.8)    | 678 (6.5)    | 208 (13.5)  | 1174 (6.0)  |
| Number of opportunities to laugh, n (%) |               |                  |                  |                    |                  |
| ≥4 Opportunities               | 562 (31.7)  | 1639 (28.9)  | 2542 (24.3)  | 278 (18.0)  | 5020 (25.8) |
| 2–3 Opportunities              | 895 (50.6)  | 3106 (54.8)  | 5736 (54.8)  | 738 (48.0)  | 10 475 (53.9) |
| <1 Opportunity                 | 314 (17.7)  | 924 (16.3)   | 2197 (21.0)  | 523 (34.0)  | 3957 (20.3) |
| Age, years, n (%)              |               |                  |                  |                    |                  |
| 65–69                           | 674 (38.1)  | 1854 (32.7)  | 3232 (30.8)  | 362 (23.5)  | 6122 (31.5) |
| 70–74                           | 468 (26.5)  | 1622 (28.6)  | 2892 (27.6)  | 354 (23.0)  | 5336 (27.4) |
| 75–79                           | 342 (19.3)  | 1289 (22.7)  | 2386 (22.8)  | 378 (24.6)  | 4395 (22.6) |
| 80–84                           | 198 (11.2)  | 638 (11.2)   | 1389 (13.3)  | 290 (18.8)  | 2515 (12.9) |
| ≥85                             | 88 (5.0)    | 266 (4.7)    | 576 (5.5)    | 154 (10.0)  | 1084 (5.6)  |
| Sex, n (%)                      |               |                  |                  |                    |                  |
| Male                            | 790 (44.6)  | 2665 (47.0)  | 4814 (46.0)  | 706 (45.9)  | 8975 (46.1) |
| Female                          | 980 (55.4)  | 3004 (53.0)  | 5657 (54.0)  | 833 (44.1)  | 10 477 (53.9) |
| Marital status, n (%)           |               |                  |                  |                    |                  |
| Married                         | 1343 (75.9) | 4293 (75.7)  | 7623 (72.8)  | 1005 (65.3) | 14 264 (73.3) |
| Widowed                         | 291 (16.5)  | 1011 (17.8)  | 2062 (19.7)  | 374 (24.3)  | 3739 (19.2) |
| Separated                       | 80 (4.5)    | 205 (3.6)    | 467 (4.5)    | 98 (6.3)    | 850 (4.4)  |
| Unmarried                       | 57 (3.2)    | 159 (2.8)    | 322 (3.1)    | 61 (4.0)    | 600 (3.1)  |
| Years of education, n (%)       |               |                  |                  |                    |                  |
| <9                              | 481 (27.2)  | 1554 (27.4)  | 3422 (32.7)  | 687 (44.6)  | 6144 (31.6) |
| 10–12                           | 749 (42.3)  | 2412 (42.5)  | 4491 (42.9)  | 551 (35.8)  | 8202 (42.2) |
| ≥13                             | 541 (30.5)  | 1703 (30.0)  | 2562 (24.5)  | 301 (19.6)  | 5107 (26.3) |
| Equivalent income, million Yen, n (%) |               |                  |                  |                    |                  |
| Low                             | 757 (42.8)  | 2520 (44.5)  | 5449 (52.0)  | 963 (62.6)  | 9690 (49.8) |
| Middle                          | 739 (41.8)  | 2436 (43.0)  | 4000 (38.2)  | 463 (30.1)  | 7638 (39.3) |
| High                            | 274 (15.5)  | 713 (12.6)   | 1025 (9.8)   | 112 (7.3)   | 2124 (10.9) |
| Depression, n (%)               |               |                  |                  |                    |                  |
| Depression                      | 194 (11.0)  | 762 (13.4)   | 2546 (24.3)  | 655 (42.6)  | 4157 (21.4) |
| No depression                   | 1576 (89.1) | 4907 (86.5)  | 7929 (75.7)  | 883 (57.4)  | 15 295 (78.6) |
| Frequency of meeting friends, n (%) |               |                  |                  |                    |                  |
| ≥2–3 days/week                  | 771 (43.6)  | 2290 (40.4)  | 3645 (34.8)  | 489 (31.8)  | 7194 (37.0) |
| <2–3 days/week                  | 999 (56.5)  | 3379 (59.6)  | 6830 (65.2)  | 1050 (68.2) | 12 258 (63.0) |
| Total participation score, n (%) |               |                  |                  |                    |                  |
| No participation                | 736 (41.6)  | 2403 (42.4)  | 4910 (46.9)  | 868 (56.4)  | 8918 (45.8) |
| 1 Organisation                 | 309 (17.5)  | 958 (16.9)   | 1837 (17.5)  | 237 (15.4)  | 3341 (17.2) |
| 2 Organisations                | 308 (17.4)  | 1003 (17.7)  | 1675 (16.0)  | 199 (12.9)  | 3185 (16.4) |
| ≥3 Organisations               | 417 (23.6)  | 1304 (23.0)  | 2053 (19.6)  | 235 (15.2)  | 4008 (20.6) |
| History of systemic comorbidities, n(%) |               |                  |                  |                    |                  |

Continued
imputations. In univariate analysis, visual status was found to be significantly associated with the frequency of laughter and the number of opportunities to laugh (p for trend <0.01). After adjusting for other covariates, significant associations remained between visual status and frequency of laughter; further, as visual status improved, ORs increased (p for trend <0.01). The adjusted OR of ‘laugh almost every day’ for individuals with excellent and very good visual status was 1.72 (95% CI 1.54 to 1.92) and 1.22 (95% CI 1.14 to 1.32), respectively, while that for those with fair/poor visual status was 0.86 (95% CI 0.76 to 0.98). Regarding the association between visual status and number of opportunities to laugh, significant associations remained; further, as visual status improved, ORs increased (p for trend <0.01). The adjusted OR of the number of opportunities to laugh (≥4) for individuals with excellent and very good visual status was 1.25 (95% CI 1.11 to 1.40) and 1.12 (95% CI 1.04 to 1.22), respectively, while that for those with fair/poor visual status was 0.87 (95% CI 0.75 to 1.01).

Similar results were observed in the sensitivity analysis with complete case data (online supplemental tables 1 and 2).

### DISCUSSION

The present study examined the association between visual impairment and laughter in the older Japanese population. Visual impairment was found to be significantly associated with laughter, both in terms of frequency as well as the number of different occasions among community-dwelling older adults. When visual status was better, both the frequency of laughter and the number of opportunities to laugh increased. Our findings suggest that improved vision may lead to laughter promotion.

Reports indicating the association between visual impairment and laughter have not been published. Considering previous studies that discussed the evolutionary meaning of laughter, our finding is not surprising. From ancient times, laughter might have been elicited by several kinds of stimulation as a reflex, and mental stimulations provoking laughter differ widely, from humour, followed by incongruous situations, relief, surprise, triumph and a sense of well-being. Some authors emphasise the social setting where the laughter occurs. In a study on preschool children in New York, among 223 situations in which laughter was observed, only 14 (6.3%) occurred when the child was alone.30 In a study on American college students, laughter increased with crowding.31
These observations contributed to a hypothesis that laughter may have evolved for its cathartic effects and adaptive value, and may have served as an evolutionary device to spread information, thwart aggression, and preserve social unity. Laughter, since its origin, seems to have not evolved as a self-contained mental response that arose when our ancestors indulged in thought, reflected on oneself, or were satisfied with their physiological need. Laughter might have evolved as a social reaction to social situations perceived by visual or auditory functions. If that is the case, it remains reasonable that the frequency and number of opportunities to laugh decrease when older adults partially lose the ability to understand social settings around them owing to visual impairment.

A population-based survey showed that 20%–50% of older adults had undetected visual decline, and that the majority of these cases were associated with refractive errors or cataracts and were, therefore, correctable. In Japan, the prevalence of diabetic retinopathy and cataracts is high, and it is estimated that at least 30% of these incidents are preventable and treatable. Therefore, the use of spectacles or low vision aids of appropriate prescription, improved access to consultation and treatment, or expanding the scope of cataract surgery could address a large portion of vision problems among older adults and pave the way for laughter promotion. Furthermore, the present study revealed that the frequency of laughter was higher in excellent/very good vision than in good vision. It is also important to improve the quality of vision and bring it closer to excellent vision, which will lead to laughter promotion. Laughter has potential physical and mental benefits, few contraindications, can be added to drug treatment, and is freely available; therefore, developing interventions that elicit laughter are attractive.

The present study has several strengths and limitations. As a strength, this is the first study to investigate the association between visual status and laughter. In addition, we used a large, population-based, data set. Because of this advantage of statistical power, we were able to adjust for various types of covariates in the analysis, including socioeconomic status, social activities, and physical health status. Our study has several limitations. First, we cannot completely exclude the possibility of reverse causation, owing to the cross-sectional nature of the data. For example, laughter may bolster human relationships by infusing communication with positive effect; therefore, people who rarely laugh may make poor impressions on others and make others less likely to help them, thus decreasing their daily happiness. Because unhappiness and poor self-rated health are highly positively correlated, those who rarely laugh might easily perceive poor self-rated health, which may produce nonadherence to health screening recommendations and treatment, and may lead to less engagement in preventive practices or self-care. Therefore, there is a possibility that those who rarely laugh lose out on the opportunity for eye checkups and treatment, which could lead to visual impairment. While there is a report of laughter-induced ophthalmic disease (laughter-induced transient vision loss in a patient with silent sinus syndrome), no laughter-induced visual impairment mechanism has, to the best of our knowledge, been reported. Second, in the present study, the types of laughter were not specified by the questionnaire. Several laughter studies distinguish between spontaneous vs simulated laughter. While spontaneous laughter is triggered by a stimulus (genuine laugh), simulated laughter is triggered by ourselves (fake laugh). Although the frequency of laughter was assessed in our study via a single question, we cannot exclude the possibility that simulated laughter was included as genuine laughter. Third, the data of the JAGES study were based on self-report, which can be subject to recall and social desirability biases. In particular, self-reported vision represents the presenting vision, not the best-corrected vision. However, self-reported vision is multidimensional and likely to encompass various aspects of vision that directly affect the daily life of older people under non-ideal conditions involving low and changing light levels, glare, and low contrast. Therefore, the data are likely highly linked with the participants’ vision-related quality of life. On the other hand, reporting may affect the results if visual status and laughter frequency are misclassified. People with a positive outlook could be more likely to report laughter and also be more likely to minimise their vision problems.

Well-being is defined by the World Health Organization-5 Well-being Index to include feeling active, relaxed, rested, interested in life and cheerful. In the present large-scale cross-sectional study, we found for the first time that visual impairment was significantly associated with decline in laughter. Improving eyesight may be helpful for laughter-provoking physical and mental benefits and a cheerful life that relates to well-being.

Author affiliations
1Department of Ophthalmology, Faculty of Medicine, Juntendo University, 2-1-1, Hongo, Bunkyo-ku, Tokyo, Japan
2Department of Ophthalmology, Juntendo University Nerima Hospital, Nerima-ku, Tokyo, Japan
3Department of Oral Health Promotion, Tokyo Medical and Dental University, Graduate School of Medical and Dental Sciences, Bunkyo-ku, Tokyo, Japan
4Department of Social Preventive Medical Sciences, Center for Preventive Medical Sciences, Chiba University, Chiba, Japan
5Department of Gerontological Evaluation, Center for Gerontology and Social Science, National Center for Geriatrics and Gerontology, Obu-city, Aichi, Japan
6Department of Ophthalmology, Juntendo University Graduate School of Medicine, Bunkyo-ku, Tokyo, Japan

Contributors Conceptualisation: AI and YH. Methodology: AI, YH, AT and JA. Investigation: YH, JA and KK. Formal analysis: YH and JA. Writing—original draft preparation: AI, YH and AT. Writing—review and editing: all authors. Supervision: JA, KK and AM. All authors read and approved the final manuscript. Guarantor: YH.

Funding This study used data from the Japan Gerontological Evaluation Study (JAGES), which was supported by the Japan Society for the Promotion of Science (JSPS) KAKENHI Gran Number (JP15H01972, JP19H03860), Health Labour Sciences Research Grant (H28-Chouju-Ippan-002), Japan Agency for Medical Research and Development (AMED) (JP17dk0110017, JP18dk0110027, JP18ls0110002, JP18ls0110009), and Research Funding for Longevity Sciences from the National Center for Geriatrics and Gerontology (29-42). This work was also...
Inoue A, Yoshimune H, Hiratsuka H. Laughter and subjective health among older adults: the JAGES prospective cohort study. J Epidemiol 2021;31:301–7.

Hayashi T, Urayama O, Kawai K, et al. Laughter regulates gene expression in patients with type 2 diabetes. Psychother Psychosom 2006;75:62–5.

Hayashi T, Urayama O, Hori M, et al. Laughter modulates proenin receptor gene expression in patients with type 2 diabetes. J Psychosom Res 2007;62:703–6.

van der Wal CN, Kook RN. Laughter-inducing therapies: systematic review and meta-analysis. Soc Sci Med 2019;232:473–88.

Black DW. Laughter. JAMA 1984;252:2995–8.

Sroufe LA, Wunsch JP. The development of laughter in the first year of life. Child Dev 1972;43:1326–44.

Privic TA, Robergs RA. Effects of Duration and Laughter on Subjective Happiness Within Different Modes of Communication. J Comput Mediat Commun 2012;17:436–50.

Wild B, Rodden FA, Grodd W, et al. Neural correlates of laughter and humour. Brain 2003;126:1211–38.

Clendon N, O’Cóllman MB, Klaiver CW, et al. Causes and prevalence of visual impairment among adults in the United States. Arch Ophthalmol 2004;122:477–85.

Yamada M, Hiratsuka Y, Roberts CB, et al. Prevalence of visual impairment in the adult Japanese population by cause and severity and future projections. Ophtalmic Epidemiol 2010;17:50–7.

Kondo K, Rosenberg M. World Health Organization. Advancing universal health coverage through knowledge translation for healthy ageing: lessons learnt from the Japan Gerontological evaluation study: lessons learnt from the Japan gerontological evaluation study. World health organization, 2018.

Whillans J, Nazroo J. Social inequality and visual impairment in older people. J Gerontol B Psychol Sci Soc Sci 2018;73:532–42.

Zimdars A, Nazroo J, Gonçal E. The circumstances of older people in England with self-reported visual impairment: a secondary analysis of the English longitudinal study of ageing (ELSA). Br J Vis Impair 2012;30:22–30.

Hayashi K, Kawachi I, Ohira T, et al. Laughter and subjective health among community-dwelling older people in Japan: cross-sectional analysis of the Japan Gerontological evaluation study cohort data. J Nerv Ment Dis 2015;203:934–42.

Wongpakaran N, Wongpakaran T, Van Reekum R. The use of GDS-15 in detecting MDD: a comparison between residents in a Thai long-term care home and geriatric outpatients. J Clin Med Res 2013;5:101–11.

Rubin DB, Schenker N. Multiple imputation for interval estimation from simple random samples with Ignorable nonresponse. J Am Stat Assoc 1986;81:366–74.

Kendermine M. Laughter in the pre-school child. Child Dev 1931;2:228–30.

Freedman JL, Perlick D. Crowding, contagion, and laughter. J Exp Soc Psychol 1979;15:295–303.

Vinciarelli A, Pantic M, Bourland H. Social signal processing: survey of an emerging domain. Image Vis Comput 2009;27:1473–59.

Evans BJW, Rowlands G. Correctable visual impairment in older people: a major unmet need. Ophthalmic Physiol Opt 2004;24:161–80.

Subramanian SV, Kim D, Kawachi I. Covariation in the subjective experience of self-rated health and happiness: a multivariate multilevel analysis of individuals and communities in the USA. J Epidemiol Community Health 2005;59:664–9.

Idler EL, Benyamini Y. Self-rated health and mortality: a review of twenty-seven community studies. J Health Soc Behav 1997;38:21–37.

Reggie SN, Kalyam K, Holds JB, et al. Laughter-induced transient vision loss in a patient with silent sinus syndrome. J Neuroophthalmol 2018;38:30–1.

Whillans J, Nazroo J, Matthews K. Trajectories of vision in older people: the role of age and social position. Eur J Ageing 2013;16:171–84.

REFERENCES

1 Fry WF. The biology of humor. Humor 1994;7:111–26.
2 Savage BM, Luan HL, Thipparthi RR, et al. Humor, laughter, learning, and health! a brief review. Adv Physiol Educ 2017;41:341–7.
3 Fry WF. The physiologic effects of humor, mirth, and laughter. JAMA 1992;267:1857–8.
4 Cousins N. Anatomy of an illness (as perceived by the patient). N Engl J Med 1976;295:1458–63.
5 Kimata H. Effect of humor on allergen-induced wheal reactions. JAMA 2001;285:738.
6 Kong M, Shin SH, Lee E, et al. The effect of laughter therapy on radiation dermatitis in patients with breast cancer: a single-blind prospective pilot study. Oncol Targets Ther 2014;7:2053–9.
7 Matsuzaki T, Nakajima I, Ishigami S, et al. Mirthful laughter differentially affects serum pro- and anti-inflammatory cytokine levels depending on the level of disease activity in patients with rheumatoid arthritis. Rheumatology 2006;45:182–6.
8 Manninen S, Tuominen L, Dunbar RI, et al. Social laughter triggers endogenous opioid release in humans. J Neurosci 2017;37:6125–31.
9 Miller M, Mangano C, Park Y, et al. Impact of cinematic viewing on endothelial function. Heart 2006;92:261–2.
10 Hayashi K, Kawachi I, Ohira T, et al. Laughter is the best medicine? A cross-sectional study of cardiovascular disease among older Japanese adults. J Epidemiol 2016;26:546–52.
11 Bressington D, Mui J, Yu C, et al. Feasibility of a group-based laughter yoga intervention as an adjunctive treatment for residual symptoms of depression, anxiety and stress in people with depression. J Affect Disord 2018;248:42–51.
12 Martin RA. Is laughter the best medicine? humor, laughter, and physical health. Curr Dir Psychol Sci 2002;11:216–20.
13 Penson RT, Partridge RA, Rudd P, et al. Laughter: the best medicine? Oncologist 2005;10:651–60.
14 Tamada Y, Takeuchi K, Yamaguchi C, et al. Does laughter predict onset of functional disability and mortality among older Japanese adults? the JAGES prospective cohort study. J Epidemiol 2021;31:301–7.
15 Hayashi T, Urayama O, Kawai K, et al. Laughter regulates gene expression in patients with type 2 diabetes. Psychother Psychosom 2006;75:62–5.
16 Hayashi T, Urayama O, Hori M, et al. Laughter modulates proenin receptor gene expression in patients with type 2 diabetes. J Psychosom Res 2007;62:703–6.
17 van der Wal CN, Kook RN. Laughter-inducing therapies: systematic review and meta-analysis. Soc Sci Med 2019;232:473–88.
18 Black DW. Laughter. JAMA 1984;252:2995–8.
19 Sroufe LA, Wunsch JP. The development of laughter in the first year of life. Child Dev 1972;43:1326–44.
20 Privic TA, Robergs RA. Effects of Duration and Laughter on Subjective Happiness Within Different Modes of Communication. J Comput Mediat Commun 2012;17:436–50.
21 Wild B, Rodden FA, Grodd W, et al. Neural correlates of laughter and humour. Brain 2003;126:1211–38.
22 Clendon N, O’Cóllman MB, Klaiver CW, et al. Causes and prevalence of visual impairment among adults in the United States. Arch Ophthalmol 2004;122:477–85.
23 Yamada M, Hiratsuka Y, Roberts CB, et al. Prevalence of visual impairment in the adult Japanese population by cause and severity and future projections. Ophtalmic Epidemiol 2010;17:50–7.