



ISSN: 0975-833X

Available online at <http://www.journalcra.com>

INTERNATIONAL JOURNAL
OF CURRENT RESEARCH

International Journal of Current Research
Vol. 11, Issue, 05, pp.4022-4026, May, 2019

DOI: <https://doi.org/10.24941/ijcr.35277.05.2019>

RESEARCH ARTICLE

EATING BEHAVIORS OF PRESCHOOL CHILDREN AND ITS RELATION TO CHILDHOOD OBESITY IN JEDDAH CITY, SAUDI ARABIA

*¹Noura Saud Alshammary, ²Sulafa Tarek Alqutub, ³Iman Mohmad Wahby Salem and ⁴Manahil Nouri

¹Department of Community Medicine, Ministry of Health, Jeddah, Saudi Arabia

²Planning Department, Saudi Commission for Health Specialties, Jeddah, Saudi Arabia

³Department of Community Medicine, King Abdulaziz University, Jeddah, Saudi Arabia

⁴Department of Preventive Medicine, Saudi Commission for Health Specialties, Jeddah, Saudi Arabia

ARTICLE INFO

Article History:

Received 10th February, 2019
Received in revised form
18th March, 2019
Accepted 14th April, 2019
Published online 30th May, 2019

Key Words:

Eating behaviors, children,
Weight, obesity risk factors,
Saudi Arabia, Jeddah.

*Corresponding author:

Noura Saud Alshammary

Copyright © 2019, Noura Saud Alshammary et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Citation: Noura Saud Alshammary, Sulafa Tarek Alqutub, Iman Mohmad Wahby Salem and Manahil Nouri, 2019. "Eating behaviors of preschool children and its relation to childhood obesity in jeddah city, Saudi arabia", International Journal of Current Research, 11, (05), 4022-4026.

ABSTRACT

Background: Obesity is not just an individual's problem but a public health issue. The healthy eating habits that are acquired in early childhood contribute to similar habits later in life and influence adult health. Therefore, young children are particularly at risk for obesity because they are fully dependent on adults for their nutritional needs both at home and school environment. **Objective:** to evaluate differences in eating behaviors according to children's weight, gender, age and parents' weight at public kindergartens in Jeddah city in Saudi Arabia. **Methods:** A cross-sectional study was carried out in public kindergartens in Jeddah city, Saudi Arabia, from October to November 2018. The Children's Eating Behavior Questionnaire (CEBQ) was used to assess eating behaviors. Measurements for height and weight were taken twice for each child and the average was used. Results: Parents of 198 children completed the questionnaire, 81.3% of children were normal weight, while 8.6% were obese. In terms of gender, the emotional undereating (EUE) was the only subscale that showed statistical difference between boys and girls, boys had a higher score (3.22 ± 0.79) than girls (2.91 ± 0.76) with p value < 0.001 . It was observed that children with excess weight had higher scores at the subscales "enjoyment of food", p value < 0.001 . **Conclusion:** The results of this study showed that children in this sample had marked obesogenic-eating behavior that are related with excess weight as well as parental weight, this behavior is considered as modifiable risk factors that needs early interventions to eliminate obesity related risk factors.

INTRODUCTION

Obesity is not just an individual's problem but a public health issue (WHO Report). In 2010, obesity was estimated to cause 3.4 million deaths globally with a 3.9% of years of life lost while 3.8% accounted for disability-adjusted life-years (DALYs) (Ng et al., 2018). Globally, the prevalence of childhood overweight and obesity grew from 4.2% in 1990 to 6.7% in 2010 with expectations to reach 9.1% by 2020 (De Onis et al., 2010). Adiposity rebound occurs between the ages of three and five. During this age period children develop the eating and physical activity behaviors that will influence their lifetime habits. Consequently, the preschool years (ages 3–5 years) have been recognized as a critical period in growth and obesity development (Barlow, 2007). The healthy eating habits that are acquired in early childhood contribute to similar habits later in life and influence adult health. Therefore, young children are particularly at risk for obesity because they are fully dependent

on adults for their nutritional needs both at home and school environment (Savage et al., 2007). When children start eating independently, which is around 4 years of age, it has been demonstrated that their weight correlates directly with their eating behaviors. Different studies demonstrated many differences in several dimensions of behavioral eating among children of various weight groups (Birch et al., 2007). Specific eating behaviors that are associated with obesity include under-responsiveness to internal satiety cues (low satiety responsiveness, high speed of eating) and over-responsiveness to external food cues such as taste, smell, availability and emotions such as high enjoyment of food, food responsiveness and emotional overeating (Barkeling et al., 1992). Several psychometric tools were developed for detecting the individual differences in behavioral eating among children which help predicts the risk of eating disorders along with obesity related problems such as the Dutch Eating Behavior Questionnaire (DEBQ) (Van Strienn and Oosterveld, 2008) and the Children's Eating Behavior Inventory (Archer et

al., 1991). One of the most comprehensive instruments in assessing the eating behavior is the Children's Eating Behavior Questionnaire (CEBQ), developed and validated in the UK targeting preschool children (Wardle *et al.*, 2001). Recently, the CEBQ has been successfully validated in many populations across the world (Spence *et al.*, 2001; Svensson *et al.*, 2001; Viana *et al.*, 2008). The CEBQ is a multi-dimensional, parent-reported questionnaire measuring children's eating behavior related to obesity risk. CEBQ contains 35 questions divided into eight subscales, so that four subscales investigate behaviors that reflect "interest in food": Food Response (FR), Enjoyment of Food (EF), Desire to Drink (DD) and Emotional Overeating (EOE). The other four subscales reflect behaviors related to "lack of interest in food": Emotional Undereating (EUE), Satiety Responsiveness (SR), Slowness in Eating (SE) and Food Fussiness (FF). CEBQ was translated and validated, for assessing eating behaviors in Saudi preschool children in Riyadh (Alhamad, 2013). The aim of this study was to evaluate differences in eating behaviors according to children's weight, gender, age and parents' weight at public kindergartens in the Jeddah city of Saudi Arabia.

MATERIALS AND METHODS

This is a cross-sectional study carried out in public kindergartens in Jeddah city, Saudi Arabia, from October to November 2018. From each of the geographical areas of Jeddah city, one kindergarten was randomly selected resulting in four kindergartens included. The children were selected from the updated student list using a systematic random sampling. The students received both the Consent forms having detailed information about the conducted study with the CEBQ to be filled in by parents and return it back to researcher. All children included in the study were between 4 to 6 years old, whose parents gave their consent to participate in the study with a total of 198 children.

In cases of unanswered questions, telephone contact was made to obtain the information from parents. At kindergartens, previously trained medical students collected anthropometric measurements of weight and height. Following CDC guideline, height was measured with a measuring non-elastic tape, height was measured as the distance between the highest point of the head and the floor and record to the nearest 0.1 centimeter (https://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/measuring_children.html). Weight was measured using an electronic weight scale, children were barefooted wearing minimal clothing, without any jackets or accessories with approximation to the nearest decimal fraction (https://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/measuring_children.html). Measurements for height and weight were taken twice for each child and the average was used. The BMI-for-age percentile growth charts were used to assess the weight status of children. After plotting the score of BMI in a relation of child's age and gender we considered, those >85 percentiles as overweight, >95 percentiles as obese, while those <85 percentiles were considered normal (Barlow, 2007). Children without anthropometric data were excluded from the sample. Data was collected and coded to be entered in the SPSS software version 25. Descriptive characteristics of the children and parents were presented by frequencies (qualitative variables). To examine associations of BMI categorization with eating behavior traits, a one-way ANOVA with post hoc test was used as well as a t test to examine age, gender and parents' weight in relation with eating behavior scale.

RESULT

Parents of 198 children completed the questionnaire with a response rate of 92%. Out of those, 81.3% of children were of normal weight while 8.6% were obese. Demographic data of children and parents is illustrated in table 1. Regarding age and gender differences in eating behaviors in accordance with mean score for CEBQ subscale, table 2 demonstrates eating behavior among gender. FR assesses eating in response to environmental food cues with a sample mean score of (male=2.52±0.81, female=2.49±0.80) with non-significance (p value = 0.25). EOE is one of the obesogenic behaviors which is an average increase in eating under negative emotions such as anger and anxiety. However, the mean EOE (male=2.14±1.24, female=2.28±1.19) and test showed non-significant association (p value=0.44). Meanwhile, DD evaluates the desire for children to drink frequently, especially sugar-sweetened drinks with results of (male=3.26±1.05, female=3.02±1.06) and a non-significance marker (p value = 0.11). Similarly, FE scores were (male=3.18±0.95, female=3.03±0.90) and a p value of 0.79. SE measuring the speed of eating during a meal and reflects a gradually reduced interest in a meal. Our result of this subscale showed a mean score of males=3.05±0.60, female=3.04±0.66 and a p value of 0.96. Moreover, SR score reflects the ability to regulate the amount of food that is eaten according to internal satiety cues, SR mean score was 3.09±0.68 for males and 3.04±0.69 for females. In terms of gender, the EUE was the only subscale that shows statistical difference between boys and girls with the male having a higher score (3.22±0.79) than the females (2.91±0.76) with a p value < 0.001.

In regards of BMI percentile differences in eating behavior, table 3 shows the eating behavior of children according to weight status. It was observed that children with excess weight had higher scores at the subscales "enjoyment of food", p value < 0.01. Children with excess weight showed increased food intake due to the emotional state when compared to the ones with normal weight. The CEBQ subscales that reflect "lack of interest in food" Slowness in Eating which assess faster eating of children that lead to gain weight and the other subscale "Satiety Responsiveness", scored low (Table 6). Lastly, table 4 and 5 illustrate how parent's weight was related to children eating behavior which played a significant factor in affecting children eating behavior. Parent's obesity showed associations with EOE and FR or EF p value < 0.01.

DISCUSSION

This study aimed to evaluate differences in eating behaviors according to children's weight, gender, age and parents' weight. Our results are consistent with other studies that used the same questionnaire (Alhamad, 2013; Passos *et al.*, 2015; Behar *et al.*, 2018). However, our FR mean score was higher than Swedish preschool children (male= 1.5, 0.4 female 1.6, 0.5) (Svensson *et al.*, 2011). These eating behaviors were found to become stronger as children get older (Webber *et al.*, 2009) while in our study we only considered children between 4 to 6 years old. Our EOE scores were similar to other study (Passos *et al.*, 2015), but was higher than a study conducted at another city of Saudi Arabia (male=1.8 (0.9), female= 1.7 (0.8)) (Alhamad, 2013) and Canada preschoolers (mean=1.63±0.53)(11), this difference may be due to different age groups between studies.

Table 1. Demographic data

Child characteristics	No.	%
Age		
4-5 years	95	48.0
5-6 years	103	52.0
Gender		
Male	97	49.0
Female	101	51.0
Weight status		
Normal weight	161	81.3
Overweight	20	10.1
Obesity	17	8.6
Parents characteristics		
Father education		
Illiterate/primary or intermediate school	26	13.1
High school and above	172	86.9
Mother education		
Illiterate/primary or intermediate school	18	9.1
High school and above	180	90.9
Father weight		
Normal weight	167	84.3
Overweight/obesity	31	15.7
Mother weight		
Normal weight	165	83.3
Overweight/obesity	33	16.7

Table 2. Eating behavior among gender

Studied Sample Items	Male	Female	Significant Tests
	Mean ± Sd	Mean ± Sd	
1.Enjoyment of food	3.18±0.95	3.03±0.90	0.25
2.Emotional overeating	2.14±1.24	2.28±1.19	0.44
3.Food responsiveness	2.52±0.81	2.49±0.80	0.79
4.Desire to drink	3.26±1.05	3.02±1.06	0.11
5.Satiety responsiveness	3.09±0.68	3.04±0.69	0.61
6.Slowness in eating	3.05±0.60	3.04±0.66	0.96
7.Emotional under eating	3.22±0.79	2.91±0.76	0.00*
8.Food fussiness	2.98±0.66	2.95±0.63	0.48

Table 3. Eating behavior of children according to weight status ANOVA test

Studied Sample Items	Normal	Overweight	obese	Significant Tests
	Mean ± Sd	Mean ± Sd	Mean ± Sd	
1.Enjoyment of food	2.95±0.84	3.53±0.69	4.05±1.26	0.00*
2.Emotional over eating	1.94±1.01	3.11±0.73	3.75±1.56	0.00*
3.Food responsiveness	2.45±0.79	2.73±0.89	2.83±0.77	0.08
4.Desire to drink	3.10±1.06	3.05±1.05	3.58±1.07	0.18
5.Satiety responsiveness	3.07±0.70	2.99±0.63	3.05±0.64	0.86
6.Slowness in eating	3.07±0.63	2.98±0.54	2.91±0.73	0.55
7.Emotional under eating	3.09±0.80	2.82±0.76	3.13±0.68	0.34
8.Food fussiness	2.97±0.63	2.97±0.72	2.72±0.63	0.28

Table 4. Eating behavior in relation to mother weight, T test

Studied Sample Items	Normal weight mother	Obese mother	Significant Tests
	Mean ± Sd	Mean ± Sd	
1.Enjoyment of food	3.10±0.95	3.15±0.79	0.00*
2.Emotional over eating	2.07±1.21	2.93±0.99	0.001*
3.Food responsiveness	2.43±0.80	2.91±0.71	0.54
4.Desire to drink	3.11±1.07	3.24±1.04	0.79
5.Satiety responsiveness	3.06±0.68	3.09±0.71	0.74
6.Slowness in eating	3.04±0.63	3.08±0.64	0.28
7.Emotional under eating	3.09±0.77	2.92±0.85	0.15
8.Food fussiness	2.96±0.61	2.91±0.78	0.24

Table 5. Eating behavior in relation to father weight, T test

Studied Sample Items	Normal weight father	Obese father	Significant Tests
	Mean ± Sd	Mean ± Sd	
1.Enjoyment of food	3.10±0.95	3.15±0.77	0.73
2.Emotional over eating	2.11±1.22	2.75±1.08	0.008*
3.Food responsiveness	2.45±0.81	2.81±0.72	0.01*
4.Desire to drink	3.17±1.09	2.96±0.88	0.26
5.Satiety responsiveness	3.06±0.69	3.06±0.66	0.97
6.Slowness in eating	3.04±0.64	3.08±0.56	0.74
7.Emotional under eating	3.10±0.76	2.89±0.89	0.24
8.Food fussiness	2.95±0.63	2.94±0.70	0.90

Table 6. Unadjusted and Adjusted Regression Analyses for CEBQ Subscales on Child

CEBQ Subscale	Unadjusted		Adjusted		
	Standardized β	Coefficient	P	Standardized β	P
1.Enjoyment of the Food	.037		$\leq .05$.350	$\leq .05$
2.Emotion Al over eating.	.038		$\leq .05$.479	$\leq .05$
3.Food responsiveness.	.010		$\geq .05$.125	$\geq .05$
4.Desire to drink	.007		$\geq .05$.057	$\geq .05$
5.Satiety responsiveness	.005		$\geq .05$.001	$\geq .05$
6.Slowness IN eating.	-.010		$\geq .05$	-.062	$\geq .05$
7.EmotionAL under eating	-.004		$\geq .05$	-.036	$\geq .05$
8.Food fusSiness	-.007		$\geq .05$	-.043	$\geq .05$

Body Mass Index (n= 198). Linear regression

Our study revealed that the mean score of DD (male=3.26±1.05, female=3.02±1.06) was similar to a study by Passos *et al.* in Brazil (Alhamad, 2013). Meanwhile, our results were higher than other studies done around the world (Passos DR dos *et al.*, 2015; Spence *et al.*, 2011; Svensson *et al.*, 2011). The mean score of DD was less than 3 which shows that Saudi preschoolers has more frequent desire to have a drink which is predisposing the children to gain more weight (Sweetman *et al.*, 2008). In relations to FE our scores were similar to other studies conducted in Brazil, Sweden and Saudi Arabia (Passos DR dos *et al.*, 2015; Svensson *et al.*, 2011; Alhamad, 2013) but was higher than the mean score of Chinese children score (Male=2.81± 0.79, female=2.87± 0.74) (Jiang *et al.*, 2014). The SR and SF represent healthy eating behaviors, the higher the score the healthier. The results of these subscales were consistent with other studies from Canada, China and Sweden (Svensson *et al.*, 2011; Alhamad, 2013; Jiang *et al.*, 2014) while in a Latin-American preschoolers scored lower in SE and SR (Behar *et al.*, 2018). Our results were in agreement with studies that showed an increase in BMI of children having increased interest in food (Santos *et al.*, 2011; Passos *et al.*, 2015; Boswell *et al.*, 2018). Furthermore, no significant difference was found between the groups of excess weight and normal weight for the subscale “Emotional Under eating”, similar to the findings of other studies (Santos *et al.*, 2011; Passos DR dos *et al.*, 2015).

Moreover, our result verified that obese children had higher scores at the subscale “Desire to Drink” than normal and overweight children but the difference was not statistically significant, p value= 0.07. Similarly, results were previously found in another study (Spence *et al.*, 2011) with p value=0.09 while a significant association was found in regards to another study conducted in Brazil (Passos DR dos *et al.*, 2015). A decrease in response to satiety makes children less capable of regulating food intake, and thus contributes to excess weight gain (Santos *et al.*, 2011; Passos DR dos *et al.*, 2015; Behar *et al.*, 2018). We couldn't observe a significant difference in the scores of the subscales “Satiety Responsiveness” and “Slowness in Eating” between children with normal weight and children with excess weight. In previous studies, it was concluded that, Satiety responsiveness was not influenced by overweight/obesity (Reyes *et al.*, 2014; Hathcock *et al.*, 2014), and no difference was found for the subscales “Food Fussiness” and “Emotional Under eating”. Our results confirms previous research on the effect of parental weight on children's eating behaviors, which is consistent for both the shared gene and shared environment theory (Llewellyn and Fildes, 2017) as well as other reports. (Alhamad, 2013; Svensson *et al.*, 2011). Lastly, comparing eating behaviors in preschool children to lean and obese parents, children with obese parents showed higher emotional overeating and food responsiveness (Wardle *et al.*, 2001).

Conclusion

The results of this study showed that children in this sample had marked obesogenic-eating behavior that are related with excess weight, this behavioris considered as modifiable risk factors that needs early interventions to eliminate obesity related risk factors. Future researches should explore the determinants of these eating behaviors and if they can be modified to reduce children's risk of becoming overweight or obese. Furthermore, parental weight played a significant role on children's eating behaviors.

Limitation

This study has some limitations that should be considered. The main limitation is that this is a cross-sectional study which limited our ability to establish cause-and-effect relations, therefore we do not know if eating behaviors are precursors or consequences of weight status. Second, parental reports of eating behavior may be subject to error because parents may have had limited opportunity to observe their child eating throughout the day. Self-reported of parents' weight may lead to underestimation.

Conflicts of interest: The authors declare no conflict of interest.

Acknowledgement

REFERENCES

- Alhamad, AH. 2013. Validation of the Children's Eating Behaviour Questionnaire (CEBQ) in the population of Saudi preschoolers. 2013 [cited 2019 Apr 9]; Available from: <https://researchcommons.waikato.ac.nz/handle/10289/8691>.
- Archer, LA., Rosenbaum, PL. and Streiner, DL. 1991. The children's eating behaviour inventory: Reliability and validity results. *J Pediatr Psychol.*
- Barkeling, B., Ekman, S. and Rössner, S. 1992. Eating behaviour in obese and normal weight 11-year-old children. *Int J Obes Relat Metab Disord.*
- Barlow, SE. 2007. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. *Pediatrics* [Internet]. 120 Suppl: S164-92. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18055651>.
- Behar, AI., Crespo, NC., Garcia, ML., Ayala, GX., Campbell, N., Shadron, LM., *et al.* 2018. Validation of a Shortened Version of the Children's Eating Behaviour Questionnaire and Associations with BMI in a Clinical Sample of Latino Children. *J Nutr Educ Behav.*

- Birch, L., Savage, JS. and Ventura, A. 2007. Influences on the Development of Children's Eating Behaviours: From Infancy to Adolescence. *Can J Diet Pract Res.*
- Boswell, N., Byrne, R. and Davies, PSW. 2018. Eating behaviour traits associated with demographic variables and implications for obesity outcomes in early childhood. *Appetite.*
- CDC. Measuring Children's Height and Weight Accurately At Home | Healthy Weight | CDC [Internet]. [cited 2018 Mar 7]. Available from: https://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/measuring_children.html.
- De Onis, M., Blössner, M. and Borghi, E. 2010. Global prevalence and trends of overweight and obesity among preschool children. *Am J Clin Nutr.*
- Hathcock, A., Krause, K., Viera, AJ., Fuemmeler, BF., Lovelady, C. and Østbye, T. 2014. Satiety responsiveness and the relationship between breastfeeding and weight status of toddlers of overweight and obese women. *Matern Child Health J.*
- Herle, M., Fildes, A., Steinsbekk, S., Rijdsdijk, F. and Llewellyn, CH. 2017. Emotional over- and under-eating in early childhood are learned not inherited. *Sci Rep.*
- Jiang, X., Yang, X., Zhang, Y., Wang, B., Sun, L. and Shang, L. 2014. Development and preliminary validation of Chinese Preschoolers' Eating Behaviour Questionnaire. *PLoS One.*
- Ng, M., Fleming, T., Robinson, M., Thomson, B., Graetz, N., Margono, C., *et al.*, 2013. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* [Internet]. 2014 Aug 30 [cited 2018 Dec 24]; 384(9945):766–81. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24880830>.
- Passos DR dos, Gigante, DP., Maciel, FV. and Matijasevich, A. 2015. Children's eating behaviour: comparison between normal and overweight children from a school in Pelotas, Rio Grande do Sul, Brazil. *Rev Paul Pediatr (English Ed).*
- Reyes, M., Hoyos, V., Martinez, SM., Lozoff, B., Castillo, M., Burrows, R., *et al.*, 2014. Satiety responsiveness and eating behaviour among Chilean adolescents and the role of breastfeeding. *Int J Obes.*
- Santos, JL., Ho-Urriola, JA., González, A., Smalley, S V., Domínguez-Vásquez, P., Cataldo, R., *et al.*, 2011. Association between eating behaviour scores and obesity in Chilean children. *Nutr J.*
- Savage, JS., Fisher, JO. and Birch, LL. 2007. Parental influence on eating behaviour: Conception to adolescence. In: *Journal of Law, Medicine and Ethics.*
- Spence, JC., Carson, V., Casey, L. and Boule, N. 2011. Examining behavioural susceptibility to obesity among Canadian pre-school children: The role of eating behaviours. *Int J Pediatr Obes.*
- Svensson, V., Lundborg, L., Cao, Y., Nowicka, P., Marcus, C. and Sobko, T. 2011. Obesity related eating behaviour patterns in Swedish preschool children and association with age, gender, relative weight and parental weight - factorial validation of the Children's Eating Behaviour Questionnaire. *Int J Behav Nutr Phys Act.*
- Sweetman, C., Wardle, J. and Cooke, L. 2008. Soft drinks and "desire to drink" in preschoolers. *Int J Behav Nutr Phys Act.*
- Van Strien, T. and Oosterveld, P. 2008. The children's DEBQ for assessment of restrained, emotional, and external eating in 7- to 12-year-old children. *Int J Eat Disord.*
- Viana, V., Sinde, S. and Saxton, JC. 2008. Children's Eating Behaviour Questionnaire: Associations with BMI in Portuguese children. *Br J Nutr.*
- Wardle, J., Guthrie, C., Sanderson, S., Birch, L. and Plomin, R. 2001. Food and activity preferences in children of lean and obese parents. *Int J Obes.*
- Wardle, J., Guthrie, CA., Sanderson, S. and Rapoport, L. 2001. Development of the Children's Eating Behaviour Questionnaire. *J Child Psychol Psychiatry.*
- Webber, L., Hill, C., Saxton, J., Van Jaarsveld, CHM. and Wardle, J. 2009. Eating behaviour and weight in children. *Int J Obes.*
- WHO. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser [Internet]. 2000; 894:1–253. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/11234459>.
