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Autism spectrum disorder in children with Type 1 diabetes

K. E. Bethin[1], **L. G. Kanapka**[2], **L. M. Laffel**[3], **S. Majidi**[4], **N. S. Chaytor**[5], **S. MacLeish**[6], **R. Adams**[7], **N. C. Foster**[2] **T1D Exchange Clinic Network**

[1]School of Medicine and Biomedical Sciences, University at Buffalo Jacobs, Buffalo, NY

[2]Jaeb Center for Health Research, Tampa, FL

[3]Joslin Diabetes Center, Boston, MA

[4]Barbara Davis Center for Diabetes, Aurora, CO

[5]Elson S. Floyd College of Medicine, Washington State University, Spokane, WA

[6]Rainbow Babies and Children's Hospital

[7]University Hospitals Cleveland Medical Center, Cleveland, OH, USA

Abstract

Aim—Links between autism spectrum disorder (ASD) and autoimmune diseases, including Type 1 diabetes have been proposed. This study assessed the frequency of ASD in children with Type 1 diabetes in the T1D Exchange (T1DX) registry and the impact of ASD on characteristics of children with Type 1 diabetes.

Methods—Analysis included 10 032 participants aged < 18 years (median Type 1 diabetes duration 6.5 years, 48% female, 77% non-Hispanic White). Diagnosis of ASD was defined as autism, Asperger's or pervasive developmental disorder.

Results—A diagnosis of ASD was recorded for 159 (1.58%) participants. Those with ASD were predominantly male (88% vs. 51% of those without ASD, $P < 0.001$) and slightly older (median 14 vs. 13 years, $P = 0.022$). Occurrence of diabetic ketoacidosis at Type 1 diabetes diagnosis was similar (35% vs. 41%, $P = 0.161$). Pump use was lower in those with ASD (51% vs. 63%, $P = 0.005$) but continuous glucose monitor use was similar (24% vs. 27%, $P = 0.351$). Median HbA_{1c} was slightly lower in those with ASD [68 vs. 69 mmol/mol (8.4% vs. 8.5%), $P = 0.006$]. This difference was more pronounced after adjusting for confounders.

Conclusions—The frequency of ASD in the T1DX registry was similar to that in the general population. These data show that despite deficits in communication, occurrence of diabetic ketoacidosis was similar in youth with and without ASD. Pump use was less frequent in those with ASD, possibly due to sensory issues, although CGM use did not differ. The lower HbA_{1c} may be due to a more regimented routine with ASD. Because comorbidities such as ASD complicate care of patients with Type 1 diabetes, further research is needed to support these children.

Correspondence to: Lauren Kanapka. t1dstats8@jaeb.org.

Competing interests

None declared.

Introduction

Both Type 1 diabetes and autism spectrum disorder (ASD) are common chronic conditions that may present during childhood [1]. Both conditions have increased significantly in prevalence over the past several decades [2–6]. The prevalence of Type 1 diabetes has increased from 1 in 670 in 2001 to 1 in 515 in 2009 (30% increase in 8 years), while the estimated prevalence of ASD in the USA has increased from 1 in 68 in 2012 to 1 in 59 in 2014 (15% increase in 2 years) with a male preponderance of 4:1 [3,6–8]. The rising incidence of ASD may be attributed to changes in the criteria for diagnosis, increased awareness, increased prevalence, differences in study design or all these factors [2,3]. Criteria for the diagnosis of ASD, a neurodevelopmental disorder, in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) include both a social (pragmatic) communication disorder and restricted interests and repetitive behaviours [9]. In addition, people with ASD may have disturbances in sensory function that present as sensory hypersensitivity, sensory hyposensitivity or sensory-seeking behaviour [10]. Given the high prevalence of ASD and the extra challenges facing individuals with the condition, it is important to identify with which comorbidities ASD is associated. Individuals with ASD have higher rates of comorbidities including a number of autoimmune diseases [11–19]. Some of these studies have shown an increased prevalence of ASD in children with Type 1 diabetes compared with the general population, whereas others have shown no difference. Recently, the German/Austrian Diabetes Patient Follow-Up registry (DPV) examined clinical characteristics and metabolic control in youth (1–20 years) enrolled in the DPV registry with Type 1 diabetes and ASD [20]. The DPV data did not demonstrate a difference in prevalence of ASD in the youth with Type 1 diabetes. Given the challenges faced by children with ASD, we investigated how the dual diagnoses of Type 1 diabetes and ASD affect metabolic control, treatment or presentation of diabetes. Data from the T1D Exchange Clinic Network (T1DX) demonstrate that, in the USA, very few children with Type 1 diabetes are meeting HbA_{1c} targets [21,22]. The DPV data, when controlled for age, gender, duration of diabetes and year of observation, show that Type 1 diabetes metabolic control is not affected by the additional diagnosis of ASD. However, the prevalence of ASDs is much lower in the DPV compared with the T1DX cohort [3,8,20,23].

The aims of this study were to estimate the frequency of ASD in youth with Type 1 diabetes enrolled in the T1DX registry and to assess the demographic and clinical characteristics of these youth compared with those without ASD. Specifically, does the diagnosis of ASD affect metabolic control or the treatment of Type 1 diabetes.

Participants and methods

The T1DX clinic network includes > 80 US-based paediatric and adult endocrinology practices. Details on eligibility criteria, informed consent process and data collection for the T1DX clinic registry have been published previously [22,24].

For this analysis, we included data on 10 032 T1DX clinic registry participants < 18 years old who underwent routine clinical examination between 1 June 2016 and 1 September 2017. Diagnosis of ASD was defined as a report of one or more of the following medical

conditions in the clinic chart: ASD, autism, Asperger's or pervasive developmental disorder. Pervasive development disorder includes disorders that result in delays in socialization and communication. Age, duration of diabetes, diabetes management characteristics, occurrence of diabetic ketoacidosis, occurrence of severe hypoglycaemia (defined as seizure or loss of consciousness), and diagnosis of concomitant diseases were obtained from clinic medical chart data extraction. Demographic information was reported by the participant or parent of the participant through completion of a comprehensive questionnaire.

Statistical analysis

Associations between ASD status and participant characteristics (demographic characteristics, duration of diabetes) were assessed using Fisher's exact (categorical characteristics) and Wilcoxon rank-sum tests (continuous characteristics). Multivariable regression models were used to assess the association of ASD with diabetes management characteristics and the diagnosis of concomitant diseases. Where appropriate, the following factors were assessed for potential confounding with each outcome through a stepwise selection procedure: age, duration of diabetes, sex, race/ethnicity, socio-economic status and device use.

Data analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA). In view of the multiple comparisons, only *P*-values < 0.01 were considered statistically significant.

Results

Among the 10 032 participants, 159 (1.58%) had a diagnosis of ASD. Participants with ASD were slightly older (median 14 vs. 13 years, $P = 0.022$) and were more likely to be male (88% vs. 51%, $P < 0.001$) than those without ASD. (Table 1). A diagnosis of ASD was not associated with race/ethnicity, socio-economic status or diabetes duration ($P \geq 0.10$ for all).

Frequency of diabetic ketoacidosis at diagnosis was similar in participants with ASD and those without (35% vs. 41%, respectively, $P = 0.161$), as shown in Table 1. Similarly, post diagnosis, the occurrences of diabetic ketoacidosis and severe hypoglycaemia within the past 12 months were not associated with ASD status ($P = 0.426$ and 0.410, respectively).

Participants with ASD were less likely to use an insulin pump (52% vs. 63%, respectively, $P = 0.005$); however, there was no difference in continuous glucose monitor (CGM) use (24% vs. 27% in participants without ASD, $P = 0.351$).

The difference in HbA_{1c} between those with and without ASD was confounded by the significant difference in pump use and age between the two groups. Therefore, although the overall median HbA_{1c} was only slightly lower [68 vs. 69 mmol/mol (8.4% vs. 8.5%)] in participants with ASD compared with those without, this difference was significant after adjusting for confounders ($P = 0.006$). Among those using both CGM and a pump, median HbA_{1c} was 58 vs. 64 mmol/mol (7.5% vs. 8.0%) in those with and without ASD, respectively (Table 2). Among adolescents aged 13 years or over, HbA_{1c} was 69 mmol/mol (8.5%) in those with ASD compared with 73 mmol/mol (8.8%) in those without (Table 3).

The median number of blood glucose checks/day was higher (4.2 vs. 4.0, $P = 0.011$) and mean total cholesterol tended to be lower (4.06 vs. 4.36 mmol/mol, $P = 0.070$) in participants with ASD compared with those without. ASD status was not associated with total daily dose of insulin/kg or concomitant thyroid or coeliac disease (Table 1). Table 3 summarizes the characteristics of the subgroups of children (<13 years) and adolescents (≥13 years) by ASD diagnosis.

Discussion

Because youth with Type 1 diabetes visit a healthcare provider more frequently than healthy youth, one would expect that ASD might be diagnosed more often in youth with Type 1 diabetes. However, at 1.58%, the frequency of ASD in T1DX participants was similar to the general US population rate of 1.69% [3,8]. The DPV data also demonstrated a similar frequency of ASD in those with Type 1 diabetes compared with the general population (0.24% vs. 0.38%, respectively). However, the frequency of ASD in the German/Austrian population is 0.38%, much lower than in the USA [23]. Interestingly, our data show a male to female ratio of 7.4:1 in participants in the T1DX compared with 4:1 in the general US population for ASD diagnosis [3,8]. The DPV data showed a 5.8:1 ratio of males to females in youth with ASD and Type 1 diabetes compared with a 2–3:1 ratio of males to females in the general German population with ASD [20,23].

Despite difficulties with social communication, the data from both the T1DX and DPV studies demonstrated no difference in diabetic ketoacidosis at presentation and during treatment, as well as no differences in severe hypoglycaemia events. These data may reflect increased parental involvement and monitoring of youth with ASD and Type 1 diabetes. Given the developmental challenges and mental health problems associated with ASD, it is not surprising that pump use is less frequent in those with ASD in the T1DX registry. The fact that there was no significant difference in CGM use may be a reflection of the overall low CGM use among children, or the reduced potential for safety concerns with these devices. The lower HbA_{1c}, higher number of daily blood glucose checks and trend toward lower cholesterol might suggest that those with ASD are more regimented in their diabetes and dietary management or that those with ASD are more likely to have an adult manage their diabetes through adolescence.

One major limitation of these findings is that the T1DX registry does not represent all children in the USA. The T1DX consists of more than 76 sites that were invited to participate in the registry representing 33 states [22]. Thirty-eight sites are primarily paediatric, 21 care for both paediatrics and adults, and 58 sites are academic. Also, because of the high representation of academic centres, there may be an over-representation of children with the dual diagnosis of Type 1 diabetes and ASD, or over-representation of children who are more difficult to manage. By contrast, there may also be an over-representation of families who have access to or are aware of the latest technologies. Another limitation to the interpretation of our data is the fact that the diagnosis of ASD, autism, Asperger's or pervasive developmental disorder was based on reports by the participants' families or primary care provider.

In the T1DX, the frequency of ASD is similar to the prevalence in the general US population, although with a higher male to female ratio. Our data combined with the DPV data suggest that there is not a link between ASD and Type 1 diabetes. Both sets of data showed a higher male prevalence for both ASD and Type 1 diabetes than seen in the population of ASD without Type 1 diabetes. Future studies should aim to look for a genetic link between Type 1 diabetes and ASD that would be seen only in males. Despite challenges associated with a diagnosis of ASD, these children with both ASD and Type 1 diabetes have better HbA_{1c} than children without ASD, without an increase in occurrence of diabetic ketoacidosis or severe hypoglycaemia. This may reflect increased parental involvement with these youth or may be a reflection of their tendency for increased regimentation. Future studies should evaluate the factors, whether behavioural or genetic, that may affect the better HbA_{1c} seen in children with Type 1 diabetes and ASD.

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References

1. Torpy JM, Campbell A, Glass RM. Chronic diseases of children. JAMA 2010; 303: 682–682. [PubMed: 20159879]
2. Mitka M Rising autism rates still pose a mystery. JAMA 2010; 303: 602. [PubMed: 20159865]
3. Baio J, Wiggins L, Christensen DL, Maenner MJ, Daniels J, Warren Z et al. Prevalence of autism spectrum disorder among children aged 8 years – Autism and Developmental Disabilities Monitoring Network, 11 sites, United States, 2014. MMWR Surveill Summ 2018; 67: 1–23.
4. Pettitt DJ, Talton J, Dabelea D, Divers J, Imperatore G, Lawrence JM et al. Prevalence of diabetes in U.S. youth in 2009: the SEARCH for Diabetes in Youth Study. Diabetes Care 2014; 37: 402–408. [PubMed: 24041677]
5. Menke A, Orchard TJ, Imperatore G, Bullard KM, Mayer-Davis E, Cowie CC. The prevalence of Type 1 diabetes in the United States. Epidemiology 2013; 24: 773–774. [PubMed: 23903880]
6. Dabelea D, Mayer-Davis EJ, Saydah S, Imperatore G, Linder B, Divers J et al. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. JAMA 2014; 311: 1778–1786. [PubMed: 24794371]
7. Christensen DL, Baio J, Van Naarden Braun K, Bilder D, Charles J, Constantino JN et al. Prevalence and characteristics of autism spectrum disorder among children aged 8 years – Autism and Developmental Disabilities Monitoring Network, 11 sites, United States, 2012. MMWR Surveill Summ 2016; 65: 1–23.
8. Xu G, Strathearn L, Liu B, Bao W. Prevalence of autism spectrum disorder among US children and adolescents, 2014–2016. JAMA 2018; 319: 81–82. [PubMed: 29297068]
9. Lord C, Bishop SL. Recent advances in autism research as reflected in DSM-5 criteria for autism spectrum disorder. Annu Rev Clin Psychol 2015; 11: 53–70. [PubMed: 25581244]
10. Baum SH, Stevenson RA, Wallace MT. Behavioral, perceptual, and neural alterations in sensory and multisensory function in autism spectrum disorder. Prog Neurobiol 2015; 134: 140–160. [PubMed: 26455789]

11. McDougle CJ, Landino SM, Vahabzadeh A, O'Rourke J, Zurcher NR, Finger BC et al. Toward an immune-mediated subtype of autism spectrum disorder. Brain Res 2015; 1617: 72–92. [PubMed: 25445995]
12. Wu S, Ding Y, Wu F, Li R, Xie G, Hou J et al. Family history of autoimmune diseases is associated with an increased risk of autism in children: a systematic review and meta-analysis. Neurosci Biobehav Rev 2015; 55: 322–332. [PubMed: 25981892]
13. Kohane IS, McMurry A, Weber G, MacFadden D, Rappaport L, Kunkel L et al. The comorbidity burden of children and young adults with autism spectrum disorders. PLoS One 2012; 7: e33224. [PubMed: 22511918]
14. Iafusco D, Vanelli M, Songini M, Chiari G, Cardella F, Fifi A et al. Type 1 diabetes and autism association seems to be linked to the incidence of diabetes. Diabetes Care 2006; 29: 1985–1986.
15. Harjutsalo V, Tuomilehto J. Type 1 diabetes and autism: is there a link? Diabetes Care 2006; 29: 484–485; discussion 485. [PubMed: 16482712]
16. Freeman SJ, Roberts W, Daneman D. Type 1 diabetes and autism: is there a link? Diabetes Care 2005; 28: 925–926. [PubMed: 15793197]
17. Diaz-Beltran L, Esteban FJ, Varma M, Ortuzk A, David M, Wall DP. Cross-disorder comparative analysis of comorbid conditions reveals novel autism candidate genes. BMC Genomics 2017; 18: 315. [PubMed: 28427329]
18. Nazeen S, Palmer NP, Berger B, Kohane IS. Integrative analysis of genetic data sets reveals a shared innate immune component in autism spectrum disorder and its comorbidities. Genome Biol 2016; 17: 228. [PubMed: 27842596]
19. Jobski K, Höfer J, Hoffmann F, Bachmann C. Use of psychotropic drugs in patients with autism spectrum disorders: a systematic review. Acta Psychiat Scand 2017; 135: 8–28. [PubMed: 27624381]
20. Lemay JF, Lanzinger S, Pacaud D, Plener PL, Furst-Burger A, Biester T et al. Metabolic control of type 1 diabetes in youth with autism spectrum disorder: a multicenter Diabetes-Patienten-Verlaufsdokumentation analysis based on 61 749 patients up to 20 years of age. Pediatr Diabetes 2018; 19: 930–936. [PubMed: 29582531]
21. Wood JR, Miller KM, Maahs DM, Beck RW, DiMeglio LA, Libman IM et al. Most youth with type 1 diabetes in the T1D Exchange Clinic Registry do not meet American Diabetes Association or International Society for Pediatric and Adolescent Diabetes clinical guidelines. Diabetes Care 2013; 36: 2035–2037. [PubMed: 23340893]
22. Miller KM, Foster NC, Beck RW, Bergenstal RM, DuBose SN, DiMeglio LA et al. Current state of Type 1 diabetes treatment in the U.S.: updated data from the T1D Exchange clinic registry. Diabetes Care 2015; 38: 971–978. [PubMed: 25998289]
23. Bachmann CJ, Gerste B, Hoffmann F. Diagnoses of autism spectrum disorders in Germany: time trends in administrative prevalence and diagnostic stability. Autism 2018; 22: 283–290. [PubMed: 29671642]
24. Beck RW, Tamborlane WV, Bergenstal RM, Miller KM, DuBose SN, Hall CA. The T1D Exchange clinic registry. J Clin Endocrin Metab 2012; 97: 4383–4389.

What's new?

- Type 1 diabetes and autism spectrum disorder are common chronic diseases that present in childhood; their combined presence adds challenges to care.
- This is the first large study of the co-existence of both diseases in the USA. The data demonstrate a frequency of autism spectrum disorder in participants in a large national diabetes database that is similar to that in the general population.
- Further research on the effect autism has on the management of diabetes is needed.

Table 1.

Association between autism spectrum disorder status and participant characteristics

	Overall (*N* = 10 032)	**Autism spectrum disorder (*n* = 159)**	**No autism spectrum disorder (*n* = 9873)**	***P*-value***
Participant characteristics				
Age (years); median (Q1, Q3)	13 (10, 16)	14 (12,16)	13 (10,16)	0.022
Type 1 diabetes duration (years); median (Q1, Q3)	6.5 (4.0, 9.2)	6.8 (4.5, 9.2)	6.5 (4.0, 9.2)	0.369
Sex (men)	5184 (52)	140 (88)	5044 (51)	<0.001
Race/ethnicity				0.889
White non-Hispanic	7690 (77)	123 (78)	7567 (77)	
Black non-Hispanic	653 (7)	12 (8)	641 (7)	
Hispanic or Latino	1061 (11)	16 (10)	1045 (11)	
Other race/ethnicity	549 (6)	7 (4)	542 (6)	
Annual household income ($)				0.143
< 50 000	2421 (32)	46 (38)	2375 (32)	
50 000 to <75 000	1271 (17)	24 (20)	1247 (17)	
≥ 75 000	3820 (51)	51 (42)	3769 (51)	
Parent education				0.461
Less than high school graduate	962 (10)	14 (9)	948 (10)	
High school graduate/GED	2676 (28)	44 (29)	2632 (28)	
Associate or bachelor's degree	3716 (39)	65 (43)	3651 (39)	
Masters, professional or doctorate degree	2197 (23)	27 (18)	2170 (23)	
Insurance status				0.781
Private	6634 (71)	106 (72)	6528 (71)	
Other	2642 (28)	40 (27)	2602 (28)	
None	95 (1)	2 (1)	93 (1)	
Clinical characteristics				
Diabetic ketoacidosis present at diagnosis	3586 (41)	47 (35)	3539 (41)	0.161
≥ 1 severe hypoglycaemic event in previous 12 months	111 (1)	3 (2)	108 (1)	0.423
≥ 1 diabetic ketoacidosis event in previous 12 months	556 (6)	11 (7)	545 (6)	0.410
Pump use	6201 (63)	81 (52)	6120 (63)	0.005
CGM use	2565 (27)	38 (24)	2527 (27)	0.351
HbA_{1c}; median (Q1, Q3)				0.006
HbA_{1c} (mmol/mol)	69 (61, 81)	68 (60, 78)	69 (61, 83)	
HbA_{1c} (%)	8.5 (7.7, 9.6)	8.4 (7.6, 9.3)	8.5 (7.7, 9.7)	
Blood glucose checks per day[†]; median (Q1, Q3)	4.0 (3.0, 6.0)	4.2 (3.9, 5.0)	4.0 (3.0, 6.0)	0.011
Total cholesterol (mmol/mol); mean (SD)	4.31 (0.87)	4.06 (0.67)	4.34 (0.87)	0.070
Total daily insulin per kg; mean (SD)	0.9 (0.3)	0.9 (0.4)	0.9 (0.3)	0.790
Diagnosis of coeliac disease	789 (8)	13 (8)	776 (8)	0.408
Diagnosis of thyroid disease	1314 (13)	22 (14)	1292 (13)	0.258

Unless otherwise stated, values are given as *n* (%).

GED, General Education Diploma; CGM, continuous glucose monitoring.

[*] *P*-values for participant characteristics were calculated using Fisher's exact and Wilcoxon rank-sum tests. *P*-values for clinical characteristics were calculated using a regression model adjusted for confounders.

[†] CGM users have been excluded from blood glucose checks/day.

[‡] Participants with missing data: age (0%), Type 1 diabetes duration (0%), sex (0%), race/ethnicity (1%), annual household income (25%), parent education (5%), insurance status (7%), diabetic ketoacidosis at diagnosis (13%), ≥ 1 severe hypoglycaemic event (1%), ≥ 1 diabetic ketoacidosis event (<1%), pump use (2%), CGM use (4%), HbA_{1c} (3%), blood glucose checks/day (11%), total cholesterol (65%), celiac disease (0%), thyroid disease (0%).

Table 2.

HbA_{1c} by autism spectrum disorder status and device use

	Autism spectrum disorder		No autism spectrum disorder	
	N	**Median (Q1, Q3)**	***N***	**Median (Q1, Q3)**
Device				
Pump and CGM	26		2091	
HbA_{1c} (mmol/mol)		(54, 74)		64 (56, 72)
HbA_{1c} (%)		7.5 (7.1, 8.9)		8.0 (7.3, 8.7)
Pump only	49		3614	
HbA_{1c} (mmol/mol)		69 (64, 81)		72 (63, 83)
HbA_{1c} (%)		8.5 (8.0, 9.6)		8.7 (7.9, 9.7)
CGM only	9		340	
HbA_{1c} (mmol/mol)		62 (54, 69)		65 (57, 73)
HbA_{1c} (%)		7.8 (7.1, 8.5)		8.1 (7.4, 8.8)
None	65		2994	
HbA_{1c} (mmol/mol)		72 (64, 78)		75 (64, 90)
HbA_{1c} (%)		8.7 (8.0, 9.3)		9.0 (8.0, 10.4)

CGM, continuous glucose monitoring.

Table 3.

Participant characteristics by age group and autism spectrum disorder status

	<13 years		≥13 years	
	Autism spectrum disorder (*n* = 57)	**No autism spectrum disorder (*n* = 4097)**	**Autism spectrum disorder (*n* = 102)**	**No autism spectrum disorder (*n* = 5776)**
Age (years); median (Q1, Q3)	10 (8, 12)	10 (7, 11)	16 (14, 17)	15 (14, 16)
Type 1 diabetes duration (years); median (Q1, Q3)	5 (4, 8)	5 (3, 7)	8 (6, 10)	8 (6, 11)
Pump use; *n* (%)	33 (59)	2611 (65)	48 (48)	3509 (62)
CGM use; *n* (%)	21 (38)	1364 (35)	17 (17)	1163 (21)
HbA_{1c}; median (Q1, Q3)				
HbA_{1c} (mmol/mol)	66 (56, 76)	67 (60, 76)	69 (63, 80)	73 (63, 87)
HbA_{1c} (%)	8.2 (7.3, 9.1)	8.3 (7.6, 9.1)	8.5 (7.9, 9.5)	8.8 (7.9, 10.1)
Blood glucose checks/day; median (Q1, Q3)	5.0 (4.0, 7.0)	5.0 (4.0, 7.0)	4.0 (3.0, 5.0)	4.0 (2.0, 5.0)
Total cholesterol (mmol/mol); mean (SD)	3.95 (20)	166 (28)	158 (28)	169 (37)
Total daily insulin per kg; mean (SD)	0.8 (0.4)	0.8 (0.3)	1.0 (0.3)	0.9 (0.3)