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Diabetes Update

Vol. 2 | Issue 25 | 2021

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you "DIABETES UPDATE" which contains latest and interesting news in the field of Diabetes and Endocrinology.

- Effect of tap dance on plantar pressure, postural stability and lower body function in older patients at risk of diabetic foot
- The First Genome-Wide Association Study for Type 2 Diabetes in Youth: The ProDiGY Consortium
- Association between thyroid hormone levels and blood glucose levels

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

Effect of tap dance on plantar pressure, postural stability and lower body function in older patients at risk of diabetic foot

Diabetic foot (DF) is a common diabetic complication, and has an adverse effect on physical functionality and quality of life. The study was conducted to examine the effects of tap dance (TD) on dynamic plantar pressure, static postural stability, ankle range of motion (ROM), and lower extremity functional strength in patients at risk of diabetic foot (DF).

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This was a randomized, single-blinded, two-arm prospective study of 40 patients at risk of DF was conducted. The intervention group (n=20) received 16 weeks of TD training (60 min/session×3 sessions/week). The control group attended four educational workshops (1 hour/session×1 session/month). Plantar pressure, represented by the primary outcomes of peak pressure (PP) and pressure-time integral (PTI) over 10 areas on each foot, was measured using the Foot scan platform system. Secondary outcomes comprised static postural stability, ankle ROM and lower extremity functional strength.

Reductions in intervention group PP (right foot: mean differences=4.50~27.1, decrease%=25.6~72.0; left foot: mean differences=-5.90~6.33, decrease%=-22.6~53.2) and PTI at 10 areas of each foot (right foot: mean differences=1.00~12.5, decrease%=10.4~63.6; left foot: mean differences=0.590~25.3, decrease%=21.9~72.6) were observed. Substantial PP and PTI differences were noted at the second through fourth metatarsals, medial heel and lateral heel in the right foot. Substantial PP and PTI differences were detected at metatarsals 1 and 2 and metatarsal 2 in the left foot, respectively. Moderate training effects were found in plantar flexion ROM of both feet, lower extremity functional strength, and length of center-of-pressure trajectory with eyes closed and open ($r=0.321$-0.376, $p<0.05$).

A 16-week tap dance program can reduce plantar pressure and significantly improve ankle range of motion, lower extremity functional strength, and static postural stability.

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	Tap dance group		Control group	
	Pretest	Post-test	Pretest	Post-test
Postural stability with eyes open				
COP trajectory (mm)	183.5±122.6	125.3±46.1	174.5±66.3	152.5±40.8
EA (mm^2)	10.9±6.10	6.35±4.76	15.3±9.99	10.8±6.47*
Postural stability with eyes closed				
COP trajectory (mm)	205.9±92.0	145.0±61.5	168.5±77.0	198.4±91.7*
EA (mm^2)	11.2±7.18	6.47±5.11	9.31±9.47	11.0±8.14*
Ankle dorsiflexion				
Left	6.05±4.37	11.4±6.16	8.20±3.04	8.35±4.53
Right	6.15±2.25	10.2±5.49	8.90±3.85	8.10±7.27
Ankle plantar flexion				
Left	28.3±9.38	38.1±11.4	28.1±5.62	31.3±3.87*
Right	29.5±7.93	38.4±9.21	30.8±5.79	33.1±4.61*
FTSST	9.85±3.07	7.25±2.81	8.18±2.05	9.40±2.84*

Within-group and between-group comparisons in postural stability, ankle range of motion, and functional lower extremities

In conclusion, as a form of weight-bearing exercise that provides constant stimulation to the plantar surface, TD is tolerated for patients at risk of DF. A 16-week TD program can significantly improve ankle ROM, lower extremity functional strength, and static postural stability, whereas a longer training period is warranted to attain significant improvements in plantar pressure

Source: Zhao Y et al. BMJ Open Diabetes Res Care. 2021 Mar;9(1):e001909. doi: 10.1136/bmjdrc-2020-001909.

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The First Genome-Wide Association Study for Type 2 Diabetes in Youth: The ProDiGY Consortium

Type 2 diabetes (T2D) is a significant health burden. T2D was not thought to be relevant to youth. This paradigm has changed with the rise in obesity among youth worldwide.

Progress in Diabetes Genetics in Youth (ProDiGY) is a collaboration of two pediatric T2D studies, Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) and SEARCH for Diabetes in Youth, along with the Type 2 Diabetes Genetics Exploration by Next-generation sequencing in multi-Ethnic Samples (T2D-GENES) consortium, a large collaborative effort to find genetic variants that influence risk of T2D in adults. This study comprehensively examine the genetics of T2D in youth in ProDiGY by comparing subjects from TODAY and SEARCH with two control cohorts: adults older than 50 years of age without T2D and youth younger than 18 years of age without diabetes. This study also examined the effect of known genetic variants associated with T2D in adults in youth-onset diabetes.

This study included multiethnic collaboration of three studies (TODAY, SEARCH, and T2D-GENES) with 3,006 youth case subjects with type 2 diabetes (mean age 15.1 ± 2.9 years) and 6,061 diabetes-free adult control subjects (mean age 54.2 ± 12.4 years). After stratifying by principal component–clustered ethnicity, performed

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association analyses on ~10 million imputed variants using a generalized linear mixed model incorporating a genetic relationship matrix to account for population structure and adjusting for sex.

The study identified seven genome-wide significant loci, including the novel locus rs10992863 in PHF2 (P = 3.2 × 10−8; odds ratio [OR] = 1.23). Known loci identified in our analysis include rs7903146 in TCF7L2 (P = 8.0 × 10−20; OR 1.58), rs72982988 near MC4R (P = 4.4 × 10−14; OR 1.53), rs200893788 in CDC123 (P = 1.1 × 10−12; OR 1.32), rs2237892 in KCNQ1 (P = 4.8 × 10−11; OR 1.59), rs937589119 in IGF2BP2 (P = 3.1 × 10−9; OR 1.34), and rs113748381 in SLC16A11 (P = 4.1 × 10−8; OR 1.04).

The ProDiGY study has discovered seven genome-wide significant associations with T2D in youth.

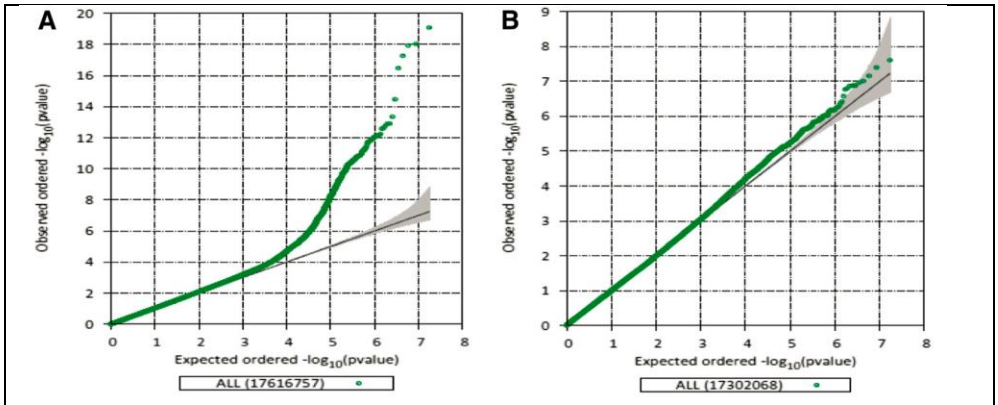

Figure: A: QQ plot for case subjects with youth-onset T2D vs. adult control subjects without diabetes. The x-axis shows the expected distribution and the y-axis shows the observed distribution of findings. lGC 5 1.08. **Figure B:** QQ plot for case subjects with youth-onset T2D vs. youth control subjects without diabetes.

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Secondary analysis with 856 diabetes-free youth control subjects uncovered an additional locus in CPEB2 (P = 3.2 × 10−8; OR 2.1) and consistent direction of effect for diabetes risk.

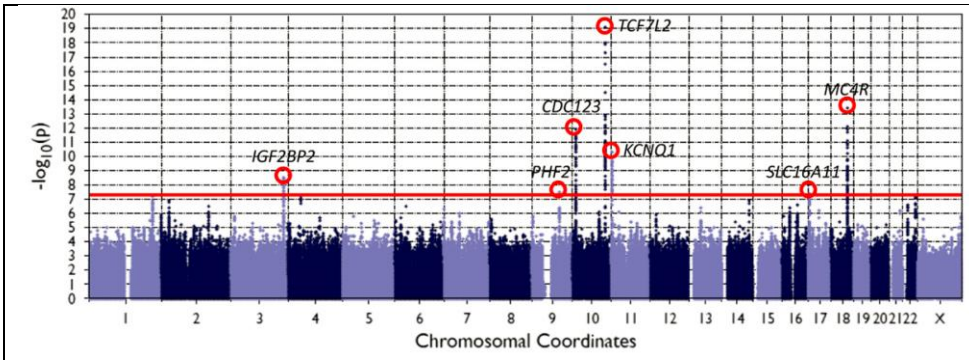

Figure 2—Manhattan plot for youth case subjects with T2D vs. adult control subjects without diabetes. The red horizontal line in the plot indicates the genome-wide significance P value threshold of 5 x 10^8. The closest genes for the seven genome-wide significant findings are shown circled in red.

In conclusion, The ProDiGY study has discovered seven genome-wide significant associations with T2D in youth, one novel and the remaining known, providing initial insight into the genetic architecture of T2D in youth. Importantly, ProDiGY has established a cohort of subjects with youth-onset T2D who serve as a valuable resource for future genetic investigation.

Source: Srinivasan S et al. Diabetes. 2021 Apr;70(4):996-1005. doi: 10.2337/db20-0443. Epub 2021 Jan 21.

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Association between thyroid hormone levels and blood glucose levels

The incidence of metabolic diseases has increased significantly in recent years. Diabetes mellitus and thyroid diseases are the two most common endocrine disorders that are found to coexist. This study aimed to explore the relationship of thyroid function and glucose metabolism and to investigate the changes in thyroid function after National Metabolic Management Center (MMC) management in type 2 diabetic mellitus (T2DM).

A total of 2000 euthyroid participants from MMC in Shanghai General Hospital and a community physical examination were recruited. They were categorized into four groups: normal glucose tolerance (NGT, n = 132), prediabetes (N = 147), DM well-controlled (T2DM with glycosylated hemoglobin [HbA1c] ≤ 7%, n = 505), and DM uncontrolled (T2DM with HbA1c > 7%, n = 1216). The parameters were compared among the groups and their changes before and after MMC follow-up in DM uncontrolled group were observed. Free triiodothyronine (FT3) and free thyroxine (FT4) levels varied significantly among groups. FT3 and FT4 levels negatively correlated with HbA1c level ($P < 0.05$), and positively correlated with the estimated glucose disposal rate (eGDR) ($P < 0.05$). Following MMC management, blood glucose and insulin resistance in the DM uncontrolled group were dramatically improved ($P < 0.001$). Meanwhile, FT3 was elevated compared to the baseline (from 4.51 ±

Low free thyroid hormone levels in normal range were significantly associated with high glucose level and severe insulin resistance

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0.78 pmol/L to 4.68 ± 0.87 pmol/L, P < 0.05), and reverse triiodothyronine (r-T3) decreased from 1.03 ± 0.24 nmol/L to 0.92 ± 0.25 nmol/L (P < 0.001). Thyroid-stimulating hormone significantly decreased as well (P < 0.001).

	Model	BMI		WHR		FPG		PPG		HbA1c		FINS		PINS		eGDR	
		β	*P*	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*
FT3	1	0.030	0.185	-0.006	0.782	**-0.070**	**0.002**	**-0.054**	**0.017**	**-0.091**	**0.000**	-0.023	0.360	0.032	0.202	**0.057**	**0.011**
	2	0.024	0.293	-0.006	0.783	**-0.064**	**0.005**	**-0.046**	**0.043**	**-0.081**	**0.000**	-0.031	0.213	0.022	0.381	**0.051**	**0.023**
	3	0.024	0.293	0.000	0.999	**-0.058**	**0.009**	-0.042	0.062	**-0.071**	**0.001**	-0.027	0.279	0.022	0.398	**0.046**	**0.041**
	4	-	-	-0.007	0.744	**-0.059**	**0.009**	-0.042	0.066	**-0.070**	**0.002**	-0.024	0.341	0.022	0.379	**0.047**	**0.035**
	5	-	-	-	-	**-0.065**	**0.004**	-0.045	0.052	**-0.070**	**0.002**	-0.024	0.350	0.021	0.408	**0.086**	**0.000**
FT4	1	-0.044	0.052	-0.039	0.086	-0.033	0.138	**-0.060**	**0.008**	**-0.075**	**0.001**	**-0.093**	**0.000**	-0.028	0.266	0.017	0.450
	2	**-0.049**	**0.029**	-0.038	0.094	-0.028	0.218	**-0.052**	**0.022**	**-0.066**	**0.003**	**-0.098**	**0.000**	-0.034	0.177	0.012	0.602
	3	**-0.049**	**0.029**	-0.029	0.203	-0.020	0.372	**-0.047**	**0.039**	**-0.052**	**0.021**	**-0.096**	**0.000**	-0.035	0.169	0.004	0.841
	4	-	-	-0.011	0.615	-0.019	0.385	**-0.048**	**0.033**	**-0.055**	**0.015**	**-0.074**	**0.003**	-0.024	0.338	0.002	0.923
	5	-	-	-	-	-0.015	0.516	**-0.049**	**0.031**	**-0.051**	**0.023**	**-0.067**	**0.008**	-0.013	0.627	**0.049**	**0.029**
TSH	1	0.020	0.371	-0.011	0.636	-0.012	0.592	-0.004	0.869	-0.012	0.595	-0.016	0.522	-0.036	0.151	0.015	0.506
	2	0.020	0.361	-0.011	0.641	-0.012	0.578	-0.004	0.849	-0.013	0.564	-0.014	0.571	-0.035	0.167	0.020	0.379
	3	0.020	0.360	-0.016	0.485	-0.018	0.433	-0.008	0.721	-0.023	0.298	-0.018	0.486	-0.035	0.173	0.025	0.270
	4	-	-	-0.240	0.280	-0.018	0.427	-0.008	0.738	-0.022	0.324	-0.032	0.209	-0.041	0.109	0.026	0.248
	5	-	-	-	-	-0.010	0.655	-0.003	0.898	-0.016	0.471	-0.029	0.259	-0.037	0.150	0.018	0.434

Relationship between thyroid hormones and metabolic parameters.

In summary, the study reported that low free thyroid hormone levels in normal range were significantly associated with high glucose level and severe insulin resistance. For poorly controlled T2DM, MMC one-year standardized management not only improved blood glucose levels, insulin resistance, and other metabolic indicators, but restored thyroid function as well.

Source: Gu L et al. J Diabetes. 2021 Apr;13(4):318-329.