and 12 cases of graft failure due to acute rejection in 2 patients and chronic rejection in 10 patients.

Blood levels of tacrolimus at 6 months and 10 years were 11.53 ng/mL and 8.72 ng/mL, respectively. Mycophenolate mofetil was used exclusively through 6 months (2000 mg/day), but by 10 years sodium mycophenolate 750 mg/day was used in 60% and mycophenolate mofetil 1250 mg/day in 40% of patients. Steroid use declined from 97% of patients at 6 months to 88% of patients at 5 years to 42% of patients at 10 years. C-peptide increased markedly from commencement of treatment in the first year and remained the same thereafter. Fasting plasma glucose and HbA1C declined at about 1 year and then remained constant. Comparisons of patients prior to surgery and at 10 years revealed significant decreases in total cholesterol and low-density lipoprotein cholesterol (LDL-C; $p<.001$ for both), with insignificant declines in high-density lipoprotein cholesterol and triglyceride.

Blood pressure (BP) measurements demonstrated significant declines from baseline in systolic BP at 1 and 5 years, and in diastolic BP only at 1 year. The left ventricular ejection fraction (LVEF) significantly increased from 54% at baseline to 59% at 10 years ($p<.001$). Kidney function declined by a mean 1.8 ± 2 mL/min annually; the overall decrease was not significant.

In this 10-year study, pancreas transplant alone was associated with satisfactory long-term patient and graft control, long-term restoration of endogenous insulin secretion and normalization of glycemic control, significant improvement in levels of total cholesterol and low-density lipoprotein, improved left ventricular ejection fraction, and a level of kidney function judged to be reasonable. Thus, the approach was concluded to be safe and effective for selected patients with T1DM.

Impaired Awareness of Hypoglycemia Mapped to Less Activation of Brain Regions Involved in Stress Response

Written by Kate Mann

Pratik Choudhary, MD, King's College London, London, United Kingdom, presented data showing that men with type 1 diabetes mellitus (T1DM) with impaired hypoglycemia awareness (HA) have different brain activation patterns than do patients with intact HA. Patients with T1DM who are unable to sense that they are hypoglycemic have less activation of brain regions involved in the stress response, autonomic activation, and emotional salience.

Hypoglycemia is a huge burden for patients with T1DM. Epidemiologic and cross-sectional studies suggest that 25% to 40% of patients with T1DM have impaired HA, and the incidence increases as the disease duration increases [Choudhary P et al. *Diabet Med* 2010]. Impaired HA increases the risk of severe hypoglycemia by 3 to 6 times [Choudhary P et al. *Diabet Med* 2010] and is associated with counterregulatory hormonal and symptomatic responses to subsequent hypoglycemia.

Dr. Choudhary and his colleagues previously published findings on the evolution of brain responses to acute hypoglycemia in nondiabetic healthy volunteers using water positron-emission tomography (PET) imaging, showing that different regions of the brain were engaged in response to different stressors [Teh MM et al. *Neuroimage* 2010]. The objective of the current study was to compare regional brain activation during experimental hypoglycemia in people with T1DM and intact or impaired HA, using radiolabeled water PET scanning. The researchers used hyperinsulinemic clamping to achieve a succession of glycemic states: euglycemia (90 mg/dL), hypoglycemia (46.8 mg/dL for 50 minutes), and recovery (90 mg/dL). Scans were performed at 10-minute intervals before, during, and up to 40 minutes after hypoglycemia.

In total, 27 right-handed men were studied (17 men with T1DM with >5 years' duration of diabetes, of whom 8 had impaired HA, and 10 healthy controls). The patients with T1DM were older and heavier than were the healthy volunteers, although those with intact and impaired HA were well matched (Table 1). A Clarke score ≥4 indicates impaired HA.

Table 1. Baseline Characteristics in Study Subjects

	Healthy Controls	Hypoglycemia Awareness	
		Intact	Impaired
Number	10	9	8
Mean age, years	27.7	37.1	35.3
Body mass index, kg/m^2	22.3	23.6	26.5
A1C, %	N/A	7.8	7.4
Diabetes duration, years	N/A	13.8	23.2
Clarke score	N/A	1.4	5.3

N/A=not applicable.

Among T1DM subjects with impaired HA compared with subjects with intact HA or healthy volunteers, acute hypoglycemia resulted in deactivation or lack of activation in brain regions involved in stress responses, autonomic activation, and emotional salience of stressful stimuli. Impaired HA resulted in activation or a lack of deactivation in areas of the brain involved in interoception, executive function, and reward and hedonic perception and in the resting state network. After recovery from hypoglycemia, there was persistent activation or lack of deactivation in reward networks in patients with impaired HA compared to those with intact HA. The investigators concluded that emotional and motivational responses to hypoglycemia, including the emotional memory of each event, are likely barriers to hypoglycemia avoidance and are potential targets for restoring HA.

Lifestyle Intervention Beneficial for Overweight and Obese Type 2 Diabetics

Written by Brian Hoyle

The multicenter Look AHEAD study [Action for Health in Diabetes; NCT0017953] is a randomized controlled clinical trial that showed that overweight and clinically obese people with type 2 diabetes mellitus who received an intensive lifestyle intervention (ILI) had statistically significant better health-related quality of life compared with controls. The findings of the present analysis were presented by Ping Zhang, PhD, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

The 5145 participants were randomly assigned to ILI (n=2570) or diabetes support and education (DSE; n=2575). The intervention included a calorie goal of 1200 to 1800 kcal/day, with <30% from fat and >15% from protein, with use of meal-replacement products, and with at least 175 minutes of moderate-intensity physical activity per week. DSE was a more traditional approach, involving support and education. The primary objective of the main trial was to compare the long-term effects on cardiovascular morbidity and mortality, while this analysis assessed the impact on quality of life as measured by health utility scores (HUSs). Effects were measured directly with a feeling thermometer (FT) and indirectly with the Health Utility Index 2 and 3 (HUI-2 and HUI-3) and the SF-6D. The FT is an established measurement based on an imaginary scale of 0 to 100, with 0 being the worst health imaginable and 100 the best with respect to the respondent's view of his or her health on that day. The SF-6D is a classification for describing health as derived from 11 items of the SF-36 questionnaire. These instruments allowed the assessment of a variety of physical, cognitive, emotional, and social well-being. The study enrolled participants from 2001 to 2004. The median follow-up was 9.67 years, and the intervention was stopped in September 2012. HUI-2, HUI-3, and SF-6D data were collected every 6 months for the first 4 years and annually thereafter, with FT data collected every 6 months throughout follow-up. Analyses of the HUSs were on an intention-to-treat basis and included differences in the mean scores overall and at the time of each data collection. Covariates included clinic site, baseline HUS, and year. Significance was indicated by $p<.05$.

The participants were well matched at baseline for sex, age, body mass index, duration of diabetes, prevalence of insulin use, A1C (glucose) level, and history of cardiovascular disease (CVD; $p>.06$ for each parameter). The completion rate for the assessments was good, ranging from ~78% to 93% depending on the assessment tool (Table 1).

Table 1. Average Completion Rates of Study Assessments, %

	DSE	ILI
HUI-3	78.3	79.4
HUI-2	82.2	82.9
SF-6D	91.7	92.2
FT	92.3	92.7

DSE=diabetes support and education; FT=feeling thermometer; HUI=Health Utility Index; ILI=intensive lifestyle intervention.

The HUI-2 and HUI-3 tools did not indicate a difference between the ILI and DSE arms, but a significant difference was found for ILI with the SF-6D and FT tools (Table 2). Significant differences favoring ILI were based on the mean SF-6D scores (overall difference, –0.010; 95% CI, –0.014 to –0.006; $p<.001$) and the mean FT scores (overall difference, –0.021; 95% CI, –0.026 to –0.016; $p<.001$).

Table 2. Mean Differences in Mean Health Utility Score Over the Study Period Between DSE and ILI by Measurement Tool

	DSE	ILI	Change From Baseline	p Value
HUI-3	0.779	0.782	0.004	0.349
HUI-2	0.789	0.792	0.004	0.249
SF-6D	0.763	0.773	0.010	<.001
FT	0.766	0.787	0.021	<.001

DSE=diabetes support and education; FT=feeling thermometer; HUI=Health Utility Index; ILI=intensive lifestyle intervention.

Subgroup analyses according to age, body mass index, sex, race and ethnicity, and presence or absence of CVD at baseline revealed no significant differences in mean HUSs across subgroups between the ILI and DSE approaches based on any measurement tool. Comparison of data