

# Characterizing Neurological and Psychiatric Manifestations of Niemann-Pick Disease Type C:

## Differences Across Age and Reporting Perspectives

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### Background / Rationale

Niemann-Pick disease type C (NPC) is a rare, progressive lysosomal storage disorder associated with heterogeneous neurological and psychiatric manifestations that evolve across the lifespan. Symptom presentation varies substantially by age of onset and disease stage, affecting both clinical monitoring and selection of meaningful endpoints in therapeutic development. Patient-reported and caregiver-reported outcomes provide important perspectives on symptom burden; however, proxy reporting may identify broader impairment profiles compared with self-report, particularly in pediatric and advanced disease populations. Improved characterization of neurological and psychiatric symptom patterns across age groups and respondent types is needed to support age-appropriate clinical care and perspective-sensitive assessment strategies.

### Primary Objective:

To characterize neurological and psychiatric manifestations of NPC across age-based cohorts and reporting perspectives using international survey responses, and to describe differences between adult self-report, adult caregiver-report, and pediatric caregiver-report symptom profiles.

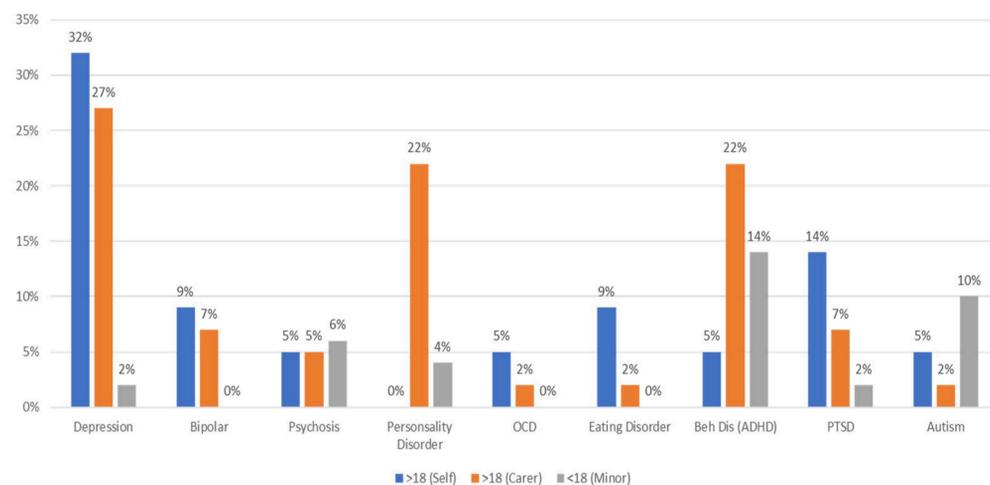
### Survey Design and Population

This preliminary analysis used data from a cross-sectional, international NPC patient and caregiver survey (N=103) conducted across 15 countries. Respondents included adults with NPC completing the survey for themselves and caregivers reporting on behalf of adult or pediatric patients. Participants were grouped as: adult self-report (n=12), adult caregiver-report (n=41), and pediatric caregiver-report (n=49). The survey captured demographic information and assessed neurological and psychiatric symptom burden across predefined categories. Results were summarized descriptively using means and proportions.

### Survey Analysis

All analyses were descriptive. Continuous variables were summarized using means, and categorical variables were summarized using proportions. Symptom patterns were compared across groups descriptively to highlight differences by age and reporting perspective.

Neuropsychiatric Symptoms



### Discussion

Neurological symptoms were near-universal across cohorts, reinforcing the pervasive neurologic burden of NPC.

Symptom profiles differed by age group: pediatric patients showed higher reporting of developmental delays and seizures, while adults more frequently reported depression and trauma-related symptoms.

Caregiver reports for adults identified greater prevalence of cognitive, speech/swallowing, and behavioral disorders compared with adult self-report.

Differences may reflect a combination of:

- true variation in disease stage and severity across cohorts
- caregiver sensitivity to functional or behavioral change
- reporting bias and limitations of proxy reporting

Age- and perspective-sensitive symptom assessment strategies may improve clinical monitoring and support therapeutic trial design.

### Survey Respondents

	Adult (>18y) (Self) (n=12)	Caregiver of Adult (n=41)	Caregiver of Minor (<18y) (n=49)
Age of Individual with NPC	38.2y	35.2y	9.8y
Age at Diagnosis (mean, IQR)	29, IQR=30.3	24.3, IQR=10.8	4.2, IQR=6.2
Sex of Individual with NPC	50% F	46% F	41%F
Sex of Respondent	---	73% F	82% F
Age of Respondent	---	61.4	41.1
Marital Status of Respondent	42% S, 50% M, 8% D	S7%, M78%, D10%	S 14%, M 90%, D 2%
Relationship to Individual with NPC	---	Mom 63%, Dad 22%, Spouse 5%, Sibling 5%, Other 5%	Mom 78%, Dad 22%
Ave Household Size	2.3 (25% have children)	2.55	3.5
Diagnosed before Birth	0	0	1
Neurologic Symptoms	92%	100%	92%

### Results and Conclusions

Neurological symptoms were nearly universal across cohorts, reported in 96% of adults completing the survey for themselves, 100% of caregiver-reported adults, and 93% of pediatric patients. The most frequently reported neurological manifestations differed by group: adult self-report most commonly identified motor and gait difficulties (33%), while caregivers of adults emphasized cognitive impairment (27%), coordination problems (22%), and speech/swallowing issues (17%). Pediatric caregiver reports most frequently cited gait/balance challenges (29%), cognitive delays (20%), motor developmental delays (16%), and seizures (14%). Multiple overlapping neurological features were common across all cohorts (18–25%), reinforcing the complex and multi-system neurologic phenotype of NPC. Neuropsychiatric symptoms also varied by age and reporting perspective.

Depression was most frequently reported among adults (32% self-report; 27% caregiver-reported adults) but was rare among minors (2%). Caregivers reporting for adults noted higher prevalence of personality disorders (22%) and ADHD (22%), whereas pediatric caregivers more frequently reported autism (10%) and ADHD (14%). Adult self-report additionally highlighted PTSD (14%) and eating disorders (9%), suggesting that certain psychiatric symptoms may be more readily identified through direct patient perspective. Across both neurological and psychiatric domains, caregiver reports frequently captured broader symptom involvement than adult self-report, potentially reflecting differences in disease severity, caregiver sensitivity to multi-domain impairment, or reporting variability by perspective. Collectively, these findings underscore the importance of incorporating multi-informant assessments when evaluating NPC symptom burden and selecting clinically meaningful endpoints.

### Conclusions and Future Directions

Survey findings demonstrate distinct neurological and psychiatric symptom profiles across age cohorts in NPC.

Pediatric caregiver reports emphasize gait/balance challenges, developmental delays, and seizures, while adults report higher depression and trauma-related symptoms. Caregiver vs self-report differences were substantial, supporting the need for multi-informant approaches to characterize NPC symptom burden in clinical practice and research.

Future research should expand sample size to increase adult self-report representation, incorporate longitudinal follow-up to characterize symptom evolution, validate survey-reported symptoms against clinician-rated and standardized measures, and evaluate associations between age at diagnosis, symptom onset, and psychiatric burden.

To learn more:

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