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Postshunt Cognitive and Functional Improvement in Idiopathic Normal Pressure Hydrocephalus

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Abstract

BACKGROUND—Improvement in gait after shunt placement has been well documented in idiopathic normal pressure hydrocephalus (iNPH); however, controversy remains regarding the extent and pattern of postsurgical cognitive changes. Conflicting findings may be explained by variability in both test selection and follow-up intervals across studies. Furthermore, most investigations lack a control group, making it difficult to disentangle practice effects from a true treatment effect.

OBJECTIVE—To examine postshunt changes in a sample of well-characterized iNPH participants compared with a group of age- and education-matched healthy control subjects.

METHODS—We identified 12 participants with iNPH undergoing shunt placement and 9 control participants. All participants were evaluated with comprehensive neuropsychological testing and standardized gait assessment at baseline and were followed up for 6 months.

RESULTS—Repeated-measures analysis of variance revealed a significant group- (iNPH and control) by-time (baseline and 6 months) interaction for Trailmaking Test B: ($P < .003$) and Symbol Digit Modalities ($P < .02$), with greater improvement in iNPH participants relative to control subjects. In addition, the iNPH group showed greater improvement in gait ($P < .001$) and caregivers reported improved activities of daily living ($P < .01$) and reduced caregiver distress ($P < .01$).

CONCLUSION—This study demonstrates improvements in mental tracking speed and sustained attention 6 months after shunt placement in iNPH. The present investigation is the first study to use a controlled design to show that cognitive improvement in iNPH is independent of practice effects. Furthermore, these findings indicate functional and quality-of-life improvements for both the shunt responder and their caregiver.

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Keywords

Cognition; Neuropsychology; Normal pressure hydrocephalus; Ventriculoperitoneal shunt

Idiopathic normal pressure hydrocephalus (iNPH) is a syndrome characterized by disturbed gait, cognition, and urinary symptoms in the context of enlargement of the ventricular system. Typically, gait impairment is the most prominent feature, yet cognitive decline can predate other symptoms and contribute to functional impairments.[1] The cognitive profile of iNPH is generally characterized by frontal-systems dysfunction, which includes executive deficits, compromised learning and recall, and reduced information processing and psychomotor speed.

Improvement in gait has been well documented after shunt placement,[2,3] yet controversy remains regarding the extent and pattern of postsurgical cognitive changes. Some studies report no change in mental status; others suggest improvement in up to 90% of patients.[4–7] Conflicting findings may be explained by variations in the depth of cognitive examination, the way in which cognitive improvement is defined, and study follow-up intervals. Furthermore, most investigations lack a control group, making it difficult to disentangle practice effects from a true treatment effect. One recent study on iNPH treatment response used comparison data from a control sample and found that iNPH patients improved on most tasks; however, effects of prior exposure to test material could not be examined because the control subjects were tested at only 1 time point.[7]

Neuropsychological test performance can change as a result of measurement error, statistical considerations (ie, regression to the mean), or the effects of prior exposure to the testing material (ie, practice effects). Although the use of alternative test forms can alleviate some concerns regarding repeat testing, the most rigorous methodology involves a controlled study design in which both patients and control subjects undergo repeat assessment. We sought to examine postshunt changes in a sample of well-characterized iNPH participants compared with a group of age- and education-matched healthy control subjects.

METHODS

Participants

Twelve participants diagnosed with probable iNPH according to published consensus criteria were recruited from an outpatient neurology service.[8] All iNPH participants were treated with a programmable valve; postsurgical shunt adjustments were at the discretion of the treating physician. Nine healthy control participants, matched on age and education, were recruited from the community. Exclusion criteria consisted of history of major neurological or psychiatric conditions that could potentially affect cognition.

Procedure

All participants provided informed consent to participate in an Institutional Review Board–approved protocol. Standardized gait evaluation[9] and comprehensive neuropsychological assessment (described in detail elsewhere[10]) were conducted at baseline (preshunt) and 2 weeks, 3 months, and 6 months after surgery. Healthy control subjects underwent testing at the same intervals. Questionnaires were completed by iNPH caregivers to assess activities of daily living (ADL[11,12]) and neuropsychiatric symptoms (Neuropsychiatric Inventory Questionnaire [NPIQ][13]). Patients also completed a brief quality-of-life (QOL) inventory (Short Form-12[14]).

Statistical Analysis

Independent-sample *t* tests (continuous variables) and χ^2 tests (ordinal variables) were used to examine demographic and baseline group characteristics. For the main analyses, 2 × 2 repeated-measures analysis of variance (ANOVA) was used to assess performance on all cognitive and gait outcome measures. Group (iNPH and control subjects) and time (baseline and 6 months) served as independent variables, and the main effects and interactions between these variables were examined. Seventeen separate analyses were conducted, and the α level was adjusted to control for inflated type I error ($P < .003$). To determine whether the changes in gait and cognition observed after shunt placement in the iNPH group translated into improvement in adaptive functioning and QOL, paired *t* tests were used to compare preshunt and postshunt responses on the functional scales. Secondary analyses were conducted to assess outcome at intermediate study intervals (2 weeks and 3 months). Correlational analyses were also used to assess the relationship between percent change in cognitive and gait measures at each time point.

RESULTS

Independent-sample *t* tests and χ^2 tests revealed no significant differences between groups on any demographic characteristics. As expected, mental status screening was significantly lower for the iNPH group compared with healthy control subjects ($P < .03$).

Independent 2 × 2 repeated-measures ANOVA revealed a group-by-time interaction for mental tracking speed and set shifting (Trailmaking Test B, $P < .003$) and gait (Gait Scale, $P < .001$), with greater improvement from baseline to 6 months in the iNPH group (Table). A similar trend was noted for processing speed and sustained attention (Symbol Digit, $P < .02$). A main effect of time was revealed for phonemic verbal fluency (FAS, $P < .001$) and motor precision (line tracing time, $P < .001$), with better performance at 6 months. Paired *t* tests within the iNPH group comparing baseline and 6-month functional outcomes revealed more independence in independent ADLs (baseline mean = 1.54, SD = 1.86; 6-month mean = 3.27, SD = 2.76; $P < .01$) and a reduction in NPIQ–Severity (baseline mean = 10.42, SD = 6.02; 6-month mean = 3.42, SD = 3.64; $P < .02$) and NPIQ–Caregiver Distress (baseline mean = 11.57, SD = 6.75; 6-month mean = 1.86, SD = 2.96; $P < .01$). Both mental (baseline mean = 48.50, SD = 13.95; 6-month mean = 52.60, SD = 7.81) and physical (baseline mean = 33.20, SD = 8.70; 6-month mean = 42.05, SD = 8.42) aspects of QOL improved 6 months after surgery, but these values did not reach statistical significance.

Exploratory analyses (α set at 0.05) included 2 × 2 repeated-measures ANOVA to assess outcome at the intermediate study intervals (2 weeks and 3 months). Group-by-time interactions were observed for mental tracking and set shifting at both 2 weeks (TMT B, $P < .003$) and 3 months (TMT B, $P < .005$), with greater improvement in the iNPH group. A group-by-time interaction for gait was observed at 3 months (Gait Scale, $P < .005$), with greater improvement in the iNPH group. A trend for gait improvement was also noted at 2 weeks (Gait Scale, $P < .07$).

Correlational analyses revealed an association between Symbol Digit and Gait Scale percent change at 2 weeks ($r^2 = 0.79$; $P < .04$); however, similar associations were not observed at 3 or 6 months. Although 2-week and 6-month Gait Scale percent change were not associated, percent change in 6-month Gait Scale was significantly correlated with both Symbol Digit ($r^2 = 0.79$; $P < .03$) and TMT B ($r^2 = .84$; $P < .04$) change at 2 weeks.

DISCUSSION

This study demonstrates that select aspects of cognition, in particular mental tracking speed and sustained attention, improve after shunt placement in iNPH. Although other investigations have shown postshunt cognitive improvement,[5–7] this study is the first to use a controlled design with age- and education-matched healthy control subjects tested at the same time intervals. This methodology provides an opportunity to disentangle true treatment effects from changes associated with repeated exposure to testing.

In the present study, shunt response was also demonstrated by improvements in gait in iNPH participants. Gait changes have been widely documented; however, this is the only published study to date that used standardized gait assessment in both iNPH and control subjects at multiple intervals. As expected, control subjects did not show any gait changes over 6 months, whereas dramatic improvements were observed in iNPH. Despite the postshunt improvement, objective scores reflect that gait is not completely restored to a level comparable to that in healthy control subjects. This is consistent with the clinical observation that a subtle degree of gait abnormality generally persists after treatment.

In addition to motor and cognitive change, postshunt functional improvement was documented by caregiver reports indicating greater independence in ADLs, reduced severity of neuropsychiatric symptoms, and reduced caregiver distress in iNPH. Although changes in QOL did not reach statistical significance, qualitative improvements in both physical and mental functions were observed. iNPH can be associated with significant functional limitations, causing affected individuals to be dependent on others for their basic needs. Our findings suggest that postshunt symptom improvement appears to translate into enhanced well-being and improved QOL for both patients and caregivers. One limitation is that the present study did not assess ADLs, neuropsychiatric symptoms, or QOL in healthy control subjects. The extent to which postshunt improvements in iNPH are expected within these domains, above and beyond normal variation, would be a fruitful area for future research.

The statistically significant differences in mental tracking and sustained attention after shunt placement are compelling in this controlled study, given the relatively small sample size. Furthermore, qualitative inspection of the data indicates that other aspects of cognition may also show clinical improvement. In our sample, there was a 41% improvement in time to completion on basic mental sequencing, as well as faster performance on tasks of manual dexterity (increased 21%) and sustained motor speed (increased 24%). This pattern is consistent with the profile of neuropsychological changes observed after the tap test,[10] a procedure often used to assess shunt candidacy. Our preliminary data suggest that these upper-extremity motor tests may be useful as sensitive markers of change after shunt placement in iNPH.

Our exploratory analyses provide preliminary information regarding the recovery curve for gait and cognition after shunt placement. We did not observe statistically significant gait improvement at 2 weeks, a finding consistent with the notion that time is needed for neurosurgical recovery before benefit from the shunt can be fully realized. However, gains in mental tracking and set shifting were observed early in the recovery process (2 weeks) and appear to be sustained for at least 6 months after surgery. Additional cognitive changes in the area of processing speed and attention were observed at 6 months and may be sustained over longer follow-up periods.

The fact that postshunt cognitive changes appear to precede clear functional recovery argues that neuropsychological measures may be sensitive and early markers of iNPH outcome. Furthermore, the association between early cognitive change and gait improvement at 6 months is particularly compelling. These data suggest that neuropsychological assessment

before and after shunt placement may provide critical information about recovery in iNPH and should be incorporated into clinical practice. Larger controlled studies with longer follow-up intervals are needed to further examine the pattern and course of cognitive recovery and to understand what changes are expected above and beyond those resulting from repeat testing.

ABBREVIATIONS

ADL	activities of daily living
ANOVA	analysis of variance
iNPH	idiopathic normal pressure hydrocephalus
NPIQ	NSight Positive Impressions Questionnaire
QOL	quality of life
TMT	Trailmaking Test

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TABLE

Sample Characteristics and Raw Scores of the Cognitive and Gait Measures at Baseline and 6 Months After Shunt Placement[a]

Demographics	iNPH Patients, n = 12	Control Subjects, n = 9
Age at baseline, y	74.92 (7.72)	73.56 (9.79)
Symptom duration, mo	26.96 (17.23)	N/A
Education, y	14.92 (2.81)	16.56 (1.94)
Sex, M/F	4/8	2/7
Handedness, R/L	11/1	8/1

Cognitive/Gait Measures	Baseline Mean (SD)	6-mo Mean (SD)	Baseline Mean (SD)	6-mo Mean (SD)
MMSE	24.50 (5.65)	25.58 (6.79)	28.50 (1.60)	29.00 (1.41)
Boston Naming	47.70 (16.45)	45.30 (21.40)	51.57 (5.44)	52.29 (6.78)
Digit Span–Total	13.33 (3.65)	13.83 (4.71)	15.25 (3.33)	16.50 (3.07)
Symbol Digit	23.44 (9.63)	32.00 (15.68)	37.13 (10.72)	38.13 (11.05)
Phonemic Fluency[b]	32.20 (15.68)	42.50 (16.19)	38.13 (11.05)	46.38 (12.24)
Semantic Fluency	11.45 (7.76)	15.00 (6.66)	16.00 (6.76)	22.38 (15.58)
HVLT-R Learning	14.82 (8.00)	17.18 (9.02)	20.50 (5.26)	23.25 (7.34)
HVLT-R Delayed Recall	3.09 (3.59)	3.82 (4.07)	6.63 (3.46)	7.13 (3.64)
TMT-A	95.56 (97.69)	56.33 (25.88)	33.00 (13.29)	31.00 (10.39)
TMT-B[c,d]	397.44 (221.93)	175.89 (170.24)	92.00 (47.65)	102.00 (54.20)
Line tracing time[b]	95.91 (30.27)	80.27 (20.91)	103.00 (31.12)	77.25 (22.84)
Serial dotting time	93.09 (59.71)	75.00 (41.04)	57.00 (20.60)	48.89 (8.18)
Finger tapping dominant	34.60 (13.01)	42.67 (10.13)	40.66 (1.91)	41.66 (6.79)
Pegboard dominant	159.41 (60.75)	124.56 (32.89)	108.88 (35.23)	97.13 (23.92)
Gait Scale[d,e,f]	21.00 (9.32)	9.67 (6.53)	6.00 (2.39)	6.25 (3.28)

[a] HVLT-R, Hopkins Verbal Learning Test–Revised; iNPH, idiopathic normal pressure hydrocephalus; MMSE, Mini Mental Status Exam; TMT, Trailmaking Test.

[b] Main effect of time, $P < .001$.

[c] Group-by-time interaction, $P < .003$.

[d] Main effect of time, $P < .003$.

[e] Group-by-time interaction, $P < .001$.

[f] Main effect of group $P < .001$.