Neuropsychological profile of children with kidney transplants

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Abstract

Background. Varying results on the cognitive outcome of children who have undergone kidney transplantation (KTx) have raised concern for specific neurocognitive difficulties.

Methods. Fifty children with KTx were assessed at a mean age of 11.1 (SD 3.2; range 6.3–16.4), on average 6.9 (SD 3.6; range 1.0–14.1) years post-operatively. A standardized test of intelligence [Wechsler Intelligence Scale for Children (WISC-III)] and neuropsychological tests from NEPSY-II were administered. The neuropsychological profile of KTx children was compared to that of a control group matched for gender, age and maternal education.

Results. The KTx children had a lower intelligence quotient (83.9) than the test norms (100.0, P < 0.001). On neuropsychological assessment, the KTx group scored generally lower than the control group did (P < 0.001). The difference was evident in both the verbal and visuospatial domains, on a sub-test of complex auditory attention, verbal working memory and facial affect recognition. When children with neurological co-morbidity were excluded, the remaining group still scored lower than the controls did on Comprehension of Instructions (P = 0.06), Design Copying (P = 0.007) and Affect Recognition (P = 0.018). A better cognitive outcome was mainly associated with the absence of neurological co-morbidity, younger age, shorter disease duration and sustained kidney function. Children with congenital nephrosis had a similar outcome to those with other diagnoses.

Conclusions. KTx children exhibit a pattern of effects in their cognitive outcome in which both the visuospatial and language domains are affected, but visual memory and simple auditory attention remain intact. Patients without neurological co-morbidity exhibit impairment in receptive language, visuospatial functions and in recognizing emotional states.

Keywords: cognitive outcome; congenital nephrosis of the Finnish type; neurodevelopment; neuropsychological test; pediatric kidney transplantation

Introduction

Studies on cognitive outcome after kidney transplantation (KTx) have reported intelligence in the low average to average range in school-age children [1–5]. The majority of patients have attended school and followed the normal curriculum [4–6]. Despite these encouraging reports, concern for specific neurocognitive difficulties lingers.

More detailed studies on neurocognitive development remain few. Falger et al. [1] found impairment in performance intelligence and motor performance among KTx children, even in the absence of neurological co-morbidity. Qvist et al. [5] found performance within the normal range in attention and executive functions, language, visuospatial processing, and memory and learning. These reports compared the performance of KTx children to normative data from test norms. Two studies have used a matched control group. Fennel et al. (1984) found greater improvement in performance intelligence and math in the KTx group than in the control group in assessments undertaken before the initiation of dialysis and 1-month post-KTx; the KTx children now reached the level of the control group. In verbal intelligence, however, both groups had very similar scores at each assessment. Additionally, no differences were found between groups at 1-year post-KTx on measures of intelligence, achievement, problem solving, verbal memory or attention. However, the groups were matched for intelligence, which explains their similar cognitive level [2]. In a more recent study, Brouhard et al. [6] found KTx children to perform significantly poorer on measures of non-verbal intelligence and achievement (spelling, reading and arithmetic) than do their siblings.

The present study aimed to evaluate comprehensively the cognitive level and neuropsychological profile of KTx children. To obtain knowledge about neurocognitive functioning in relation to age expectations, KTx children were compared to a matched control group.

Materials and methods

Children included in the study had undergone kidney or kidney–liver transplantation at least 1 year prior to assessment, attended medical
Cognitive outcome and pediatric kidney transplantation

follow-up at the Helsinki University Central Hospital (HUCH), were between 6.0 and 16.5 years of age (born between November 1991 and September 2003) and had Finnish or Swedish as their first language. Of a total of 62 patients, 2 had died post-Tx and one patient had an acute clinical condition which precluded testing. One patient whose first language was neither Finnish nor Swedish and another child with severe tetraplegia and cerebral palsy were excluded. One child was unable to complete the assessments due to psychological distress. Of the remaining 56 patients, 6 declined to participate in the study. Of the six patients who declined to participate, one had cerebral palsy, sensorineural hearing loss and attended a special school. One patient was born prematurely, had suffered from asphyxia and experienced seizures and posterior reversible leukoencephalopathy syndrome. The four remaining patients had a normal neurological outcome.

A total of 50 children (22 girls and 28 boys) who had undergone transplantation between February 1993 and January 2008 participated in the study. Two patients had received haemodialysis after a failure of peritoneal dialysis and two received haemodialysis only. The rest had received peritoneal dialysis. As many as 39 (78%) were deceased donor organ recipients. Five patients had undergone a combined liver–kidney Tx; four had a re-Tx. In two cases, the first transplant was a kidney, and the re-transplant was a combined liver–kidney. As background characteristics, variables came from the latter Tx. The immunosuppressive medication cyclosporine A was used in 24 patients and tacrolimus in 26, both in combination with methylprednisolone. In addition, most patients used either azathioprine (n = 32) or mycophenolate mofetil (n = 17). Ten patients had received growth hormone treatment. For clinical data, see Table 1. The control group was formed from the Finnish NEPSY-II standardization sample in which 923 children aged 3–15 years were assessed individually [7]. Data were collected during the years 2007–2008. The control group underwent no Wechsler Intelligence Scale for Children (WISC)-III evaluation. For each child with KTx, one child of the same gender, approximate age and maternal educational level (four levels) was randomly chosen. All children in the control group attended school with a normal curriculum, and none had any neurological diagnosis.

Table 1. Clinical data for 50 patients with kidney transplants

<table>
<thead>
<tr>
<th>Measures</th>
<th>Mean (SD)</th>
<th>Range</th>
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<tbody>
<tr>
<td>Hospital stay after KTx, days</td>
<td>30.9 (11.9)</td>
<td>18.0 to 64.0</td>
</tr>
<tr>
<td>Intensive care unit stay after KTx, days</td>
<td>2.3 (0.8)</td>
<td>1.0 to 5.0</td>
</tr>
<tr>
<td>GFR, mL/min/1.73 m²</td>
<td>47.5 (14.8)</td>
<td>14.0 to 88.0</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>98.7 (62.3)</td>
<td>38.0 to 452.0</td>
</tr>
</tbody>
</table>

Procedure

The ethics review board at HUCH approved the study. Written consent came from one caregiver of each child. The children were recruited for the study during their annual re-evaluation visit to HUCH or an appointment was made by telephone to assess the child at the hospital closest to home. The first author and two trained psychology students performed the assessments between May 2007 and September 2009. At the time of assessment, all patients were medically stable but had a weakened kidney function; 19% had values near normal [glomerular filtration rate (GFR) > 60 mL/min/1.73 m²] and 81% below normal (GFR < 60 mL/min/1.73 m²).

The short form of the Finnish version of the WISC-III [8] served as an evaluation of cognitive capacity (the WISC-IV was not available in Finnish). Three scales were compiled: the estimated Verbal Intelligence Quotient (VIQ; sub-tests Information, Similarities and Comprehension), the Performance Intelligence Quotient (PIQ; sub-tests Picture Completion, Picture Arrangement and Block Design) and the Full-Scale Intelligence Quotient (FSIQ). One patient exceeded the age criteria and did not take the WISC-III.

The NEPSY-II [7, 9] comprises 29 sub-tests from six domains of development. According to the test manual, the selection of sub-tests is according to the child’s age and clinical needs. Ten sub-tests were administered: the Auditory Attention and Response Set (Attention and Executive Functions domain), Speeded Naming and Comprehension of Instructions (Language domain), Visuomotor Precision (Sensorimotor domain), Memory for Designs, Memory for Faces, Word List Interference (Memory and Learning domain), Design Copying and Geometric Puzzles (Visuospatial Processing domain) and Affect Recognition (Social Perception domain). These sub-tests provided a comprehensive profile across all domains. One patient did not wish to take part in the NEPSY-II assessment.

Parents also completed a form on demographic, educational and social variables. Information on medical variables and rehabilitation services came from medical records. Kidney function was evaluated as serum
creatine level (micromoles per litre) and as GFR, measured by $^{51}$Cr-
ethylenediamine tetraacetic acid (EDTA) clearance (mL/min/1.73 m$^2$).
Height was transformed to a z-score and weight was expressed as a weight
for height index (expressed as a percentage), which is a ratio to the mean index
in the normal population of the same chronological age and gender [10].

The following variables were used in correlational analyses with cog-
nitive outcome: maternal education (two levels: comprehensive school or
secondary level versus lower or higher tertiary level), premature birth
(gestational week < 37, n = 16), disease duration prior to KTx, waiting
time for KTx, total time on dialysis, age at first KTx, height at KTx, type of
transplant (deceased donor versus living donor), diagnosis of congenital
nephrosis of the Finnish type (CNF) (yes/no), time since KTx, total days of
hospitalization following KTx, time in the intensive care unit, neurological
co-morbidity or severe risk factors (yes/no), creatinine level and GFR at
the time of assessment.

**Statistical analyses**

Statistical calculations were carried out with PASW Statistics 18.0
(SPSS, Chicago, IL). Chi-square comparison and the independent sam-
ple t-test were used to compare groups with respect to background
characteristics. The WISC-III and NEPSY-II scores were in age-
corrected standard scores. The WISC-III scores were compared to the
test norms with the Student’s one-sample t-test. For the NEPSY-II, a
profile analysis was carried out using repeated measures analysis of var-
iance with the group as the independent variable and the sub-test scores as
dependent variables, thereby allowing comparison of the groups’ test
profiles (total KTx group versus control group and KTx group without
neurological co-morbidity versus control group) [11]. Missing observations
for the NEPSY-II (<5%, range 1–3) were estimated with the expectation-
maximization algorithm [12]. For the univariate analyses, P-values were
corrected using the Bonferroni correction. Medical/background variables
and outcome were analysed using the Pearson or Spearman correlation
coefficient or the independent samples t-test, as appropriate. All tests of
significance were two tailed ($P < 0.05$), and partial eta squared ($\eta_p^2$) served
as an indicator of effect size.

**Results**

**Background characteristics**

Patient and control groups did not differ with respect to gender (28 boys and 21 girls), age [KTx 11.2 (SD 3.2)
versus control group 11.0 (SD 3.0) years, $P = 0.829$] or maternal education (33 comprehensive school or secondary
level, 16 lower or higher tertiary level).

Of the 50 patients, 33 (66%) were considered to have a
normal neurological outcome and 17 patients (34%) had
neurological co-morbidity or severe risk factors post-KTx
(Table 2). Thirty-four patients (68%) attended age-
appropriate classes according to the normal curriculum.
Ten patients (20%) attended full-time special education
and seven (14%) attended part-time special education
(three in mathematics, three in mathematics and a foreign
language and one not specified). Of these patients, three
(6%) also had a postponed school start and three (6%) had
repeated a school grade.

**Global intelligence**

KTx children obtained significantly lower intelligence
scores compared to the test norms and performed in the low
average range ($<90$) (Table 3). In 27 patients (55%),
FSIQ was in the normal average range (FSIQ $\geq$ 85), except
for one who scored slightly above average (FSIQ $> 115$).
Twelve patients (24%) scored in the borderline range
(FSIQ $- 1$ SD = 70–84), and nine (18%) scored below
normal (FSIQ $- 2$ SD < 70). All of the patients with low
FSIQs were able to speak, lived with their families and
attended school (full-time or part-time special education).
All but one were ambulatory. In 17 patients (35%), PIQ
was significantly lower than VIQ (15–55 score difference),
whereas 6 patients (12%) had a significantly lower VIQ
than PIQ (15–40 score difference).

Patients with neurological co-morbidity or risk factors
had significantly lower scores than did children without
major neurological co-morbidity, particularly that affecting
PIQ (independent samples t-test: VIQ $P = 0.015$, PIQ
$P = 0.003$ and FSIQ $P = 0.005$).

**Neurocognitive test profile**

The significant between-subject effect of group, $F(1, 92) =
22.2$, $P < 0.001$, $\eta_p^2 = 0.195$, indicated that KTx children
scored generally lower than did the control group. The
interaction of test and group was significant, $F$(Green-
house-Geisser corrected $df = 8.3, 765.6$.) $= 2.3$, $P =
0.016$, $\eta_p^2 = 0.025$, indicating that the KTx and control
groups did not have parallel test profiles in the NEPSY-II.
For univariate analyses of the individual sub-test scores, see
Figure 1.

When patients with neurological co-morbidity were
excluded from the analyses, the significant between-subject
effect of group, $F(1, 77) = 8.8$, $P = 0.004$, $\eta_p^2 = 0.102$.
indicated that KTx children without neurological co-
morbidities continued to score generally lower than did the
control group. On the sub-test level, significant differ-
ces were found in the Comprehension of Instructions
($P = 0.006$), Design Copying ($P = 0.007$) and Affect Rec-
ognition ($P = 0.018$) sub-tests.

**Congenital nephrosis of the Finnish type**

For a comparison of background characteristics between
children with CNF and other diagnoses, see Table 4. Of
the non-CNFP children, 86% had a congenital disease.
Risk factors

In a bivariate correlation, VIQ, PIQ, FSIQ and those NEPSY-II sub-tests that showed a significant decrease in KTx recipients were chosen as outcome measures (Table 5). The following background variables strongly intercorrelated (r): the duration of kidney disease correlates 0.967 (P < 0.001) with age at KTx and –0.448 (P = 0.001) with follow-up time. Likewise, age at KTx and follow-up time correlated –0.485 (P < 0.001).

Discussion

We found a generalized effect on cognitive development in children with kidney failure and consequent KTx.
However, visual memory and simple auditory attention remained intact. Patients without neurological co-morbidity or risk factors had intelligence in the normal range and an age-appropriate outcome in auditory attention, visual and verbal memory, verbal fluency, visuomotor precision and non-motor visual processing. Specific difficulties were seen in receptive language, visuospatial functions and affect recognition. A better outcome was mainly associated with the absence of neurological co-morbidity, shorter disease duration, younger age and a better long-term kidney function.

Global intelligence

The global intelligence score (FSIQ 84) reported in our study is poorer than that reported in other studies (87–103) [1–5]. To obtain a complete picture of the population, however, we included all children who received a KTx and who were able to attend the assessments. Consequently, a high percentage of patients fall in the cognitively delayed range (18%), even though the majority of patients scored in the normal range (55%). Many other studies have used exclusion criteria such as cognitive delay [4], retardation, seizures [13] and neurological or systemic disease [6]. The varying exclusion criteria and small group sizes may well be seen to affect the results between studies. There are also differences between the early and later patient cohorts. Owing to advances in medical care, patients today have more promising outcomes than did early patient cohorts yet even more demanding patients are being accepted for KTx.

When children with neurological co-morbidity were excluded from the analyses, FSIQ fell in the normal average range (90.6). It is worth noting that the neurological co-morbidity variable includes a diagnosis of mental retardation. Similarly, Qvist et al. [5] at our department found average intelligence in the patient group attending regular class (VIQ 92.3, PIQ 92.8), although when all KTx children were included, both values were the lowest reported to date in the paediatric KTx literature (VIQ and PIQ 87.5). Another study that included all patients [1] used median values instead of mean values. When reported as median values, our study population has an FSIQ of 89, which is still notably lower than that reported by Falger et al. (median FSIQ 97).

Neuropsychological test profile

A pattern of effects on neurocognitive development was observed in the NEPSY-II. Compared to the matched controls, difficulties emerged in both the verbal and visuospatial domains, on a sub-test of complex auditory attention, verbal working memory and the recognition of emotional states. Visual memory and simple auditory attention remained intact. Previous studies have reported problems within non-verbal reasoning, measured as a significantly lower PIQ compared to VIQ [1]. In addition, studies have reported significantly lower psychomotor development compared to mental development in 44% of pre- and 36% of post-KTx infants [14]. An early study from 1984 reported the greatest pre- to post-KTx improvement in non-verbal problem solving [2]. In our study, 35% had significantly lower PIQ compared to VIQ, yet the difference was mainly observed in the group with neurological co-morbidity and non-CNF children. However, not all studies have confirmed more difficulties in PIQ compared to VIQ [2, 5]. In CNF, in particular, Qvist et al. [5] reported equal VIQ and PIQ in a group of patients transplanted before the age of five. Our results indicate that CNF patients have shorter illness duration and early KTx, which may alleviate visuospatial impairment in particular.

Patients without neurological co-morbidity had age-appropriate outcomes in auditory attention, visual and verbal memory, visuomotor precision, verbal fluency and non-motor visual processing. Specific difficulties arose in

### Table 4. Comparison of 28 patients with CNF and 22 patients with other diagnoses

<table>
<thead>
<tr>
<th>Data</th>
<th>CNF*</th>
<th>Other*</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Birth data</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Gestational age, weeks</td>
<td>35.5 (2.3)</td>
<td>37.4 (2.3)</td>
<td>0.026</td>
</tr>
<tr>
<td>Height, cm</td>
<td>47.2 (3.0)</td>
<td>49.1 (2.2)</td>
<td>0.023</td>
</tr>
<tr>
<td>Birth weight, kg</td>
<td>2.5 (0.4)</td>
<td>3.3 (0.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pre-transplantation data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration pre-KTx, years</td>
<td>1.9 (0.9)</td>
<td>4.3 (3.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Time on dialysis, years</td>
<td>1.5 (1.1)</td>
<td>1.3 (1.2)</td>
<td>0.670</td>
</tr>
<tr>
<td>Waiting time for KTx, days</td>
<td>386 (315)</td>
<td>223 (213)</td>
<td>0.06</td>
</tr>
<tr>
<td>Transplantation data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at first KTx, years</td>
<td>1.9 (0.9)</td>
<td>5.2 (4.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight for height index at KTx, %</td>
<td>0.57 (8.5)</td>
<td>12.5 (20.7)</td>
<td>0.009</td>
</tr>
<tr>
<td>Data at time of evaluation</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Age, years</td>
<td>11.0 (3.4)</td>
<td>11.3 (3.1)</td>
<td>0.742</td>
</tr>
<tr>
<td>Follow-up time since KTx, years</td>
<td>8.2 (3.4)</td>
<td>5.8 (3.5)</td>
<td>0.016</td>
</tr>
<tr>
<td>Weight for height index, %</td>
<td>0.55 (9.0)</td>
<td>20.8 (35.3)</td>
<td>0.008</td>
</tr>
<tr>
<td>Neurological co-morbidity</td>
<td>7 (25%)</td>
<td>10 (45%)</td>
<td>0.773</td>
</tr>
</tbody>
</table>

*Data presented as mean (standard deviation).

Total time on peritoneal or haemodialysis. For patients with re-transplants, time on dialysis and waiting time for KTx includes both first and second Tx.

Percentage of patients fall in the cognitively delayed range (90.6). It is worth noting that the neurological co-morbidity variable includes a diagnosis of mental retardation.

Neuropsychological test profile - A pattern of effects on neurocognitive development was observed in the NEPSY-II. Compared to the matched controls, difficulties emerged in both the verbal and visuospatial domains, on a sub-test of complex auditory attention, verbal working memory and the recognition of emotional states. Visual memory and simple auditory attention remained intact. Previous studies have reported problems within non-verbal reasoning, measured as a significantly lower PIQ compared to VIQ [1]. In addition, studies have reported significantly lower psychomotor development compared to mental development in 44% of pre- and 36% of post-KTx infants [14]. An early study from 1984 reported the greatest pre- to post-KTx improvement in non-verbal problem solving [2]. In our study, 35% had significantly lower PIQ compared to VIQ, yet the difference was mainly observed in the group with neurological co-morbidity and non-CNF children. However, not all studies have confirmed more difficulties in PIQ compared to VIQ [2, 5]. In CNF, in particular, Qvist et al. [5] reported equal VIQ and PIQ in a group of patients transplanted before the age of five. Our results indicate that CNF patients have shorter illness duration and early KTx, which may alleviate visuospatial impairment in particular. Patients without neurological co-morbidity had age-appropriate outcomes in auditory attention, visual and verbal memory, visuomotor precision, verbal fluency and non-motor visual processing. Specific difficulties arose in
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</tr>
</thead>
<tbody>
<tr>
<td>Age at KTx</td>
<td>-0.374*</td>
<td>-0.353**</td>
<td>-0.253**</td>
<td>-0.336**</td>
<td>-0.355**</td>
<td>-0.345**</td>
<td>-0.375**</td>
<td>-0.263*</td>
<td>-0.375**</td>
<td>-0.355**</td>
<td>-0.355**</td>
<td>-0.355**</td>
<td>-0.345**</td>
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<tr>
<td>Age at assessment</td>
<td>-0.274</td>
<td>-0.284</td>
<td>-0.254</td>
<td>-0.344</td>
<td>-0.374</td>
<td>-0.353</td>
<td>-0.364</td>
<td>-0.263</td>
<td>-0.374</td>
<td>-0.354</td>
<td>-0.354</td>
<td>-0.345</td>
<td>-0.335</td>
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</tr>
<tr>
<td>Follow-up time</td>
<td>-0.102</td>
<td>-0.132</td>
<td>-0.102</td>
<td>-0.162</td>
<td>-0.202</td>
<td>-0.202</td>
<td>-0.162</td>
<td>-0.132</td>
<td>-0.202</td>
<td>-0.202</td>
<td>-0.202</td>
<td>-0.202</td>
<td>-0.162</td>
<td></td>
</tr>
<tr>
<td>GFRb, creatinine</td>
<td>-0.355**</td>
<td>-0.244</td>
<td>-0.254</td>
<td>-0.284</td>
<td>-0.374</td>
<td>-0.353</td>
<td>-0.364</td>
<td>-0.263</td>
<td>-0.374</td>
<td>-0.354</td>
<td>-0.354</td>
<td>-0.345</td>
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<tr>
<td>Neurological co-morbidity</td>
<td>-0.287*</td>
<td>-0.287*</td>
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Table 5. Correlations between cognitive outcome and selected background characteristics for 50 patients with kidney transplants

Correlations between cognitive outcome and selected background characteristics for 50 patients with kidney transplants. Data expressed as Pearson’s correlation coefficient. **P < 0.01, *P < 0.05, †P < 0.10.

Some studies have identified reduced attention as a consequence of renal failure and have noted an improvement in sustained visual attention and stimulus discrimination sensitivity from pre- to post-KTx [4]. Qvist et al. reported attention deficit in 24% of KTx recipients, yet deficits were absent on a group level. An auditory continuous performance test revealed no differences between KTx children and a control group [2]. We found lower performance in complex auditory attention and related verbal working memory in KTx children than in a control group, yet the difference did not remain in KTx children without neurological co-morbidity.

Of KTx children, 61–79% attend school according to the normal curriculum [5, 6]. However, lower achievement among children on dialysis and post-KTx than among their siblings has been reported. This difference may stem from both more days missed from school and lower intelligence scores in the patient group [6]. There is, however, an inherent difficulty in combining patients on dialysis and post-KTx. For example, an earlier study reported achievement among KTx children in regular class to be at or above their age and grade levels, whereas children on dialysis tended to score below their age and grade levels [3]. In Finland, 8.5% of comprehensive school students attend full-time special education and 23.3% attend part-time special education [17]. KTx children received notably more full-time special education (20%) but less part-time special education (14%). A major cause for part-time special education was mathematics, as was also observed in heart Tx children [18]. However, the amount of special education is less than expected from the number of KTx children with intelligence in the borderline or delayed range (42%). In addition, only three patients (6%) had diagnosed mental retardation. This is in accordance with other studies on children with solid organ Tx, where cognitive impairment and the need for interventions at school have been under-recognized [18–20].

**CNF**

Concern has grown for an adverse neurodevelopmental outcome in children transplanted for CNF [5, 21]. These patients are severely ill from birth with a lower gestational age and birth weight [22, 23] and they are transplanted significantly earlier than are children with other diagnoses.
However, their cognitive outcome is surprisingly good; they score higher on all measures than do children with other diagnoses. Interestingly, this difference approached significance in the visuospatial domain. We found no other study reporting the cognitive outcome of CNF children alone. Qvist et al. [5] reported a high percentage of neurological sequelae on MRI among the first CNF patients who received a KTx. In our study, children with CNF did not have more neurological sequelae than did non-CNF children.

Risk factors

In our study, deteriorating kidney function was associated with poorer verbal ability, verbal working memory and complex auditory attention. Deterioration of memory functions with increasing blood urea nitrogen levels or decreasing creatinine clearance has been reported [13]. Among children with chronic kidney disease without KTx, GFR was a significant predictor of intellectual and academic outcomes [24]. In some studies, kidney function among KTx recipients failed to correlate with cognitive data [1, 14]. Our patients had a poorer GFR than did patients in several previous studies [4]. However, we used measured GFR (EDTA), which yields stricter values than does estimated GFR (e.g. calculated with the Schwartz formula [25]). In addition, kidney function tends to deteriorate over time [26–28]. Although other studies have assessed patients—1 [2, 4, 14] or 6 years post-KTx [1, 5], our patients were assessed on average 7 years post-KTx.

Older age at KTx and at follow-up seem to associate negatively with cognitive outcome. Children with KTx later in life experience a longer disease duration, thus placing them at risk for more neurodevelopmental deficits. However, the strongest association occurred between neurological co-morbidity and poorer outcome observed on all sub-tests of the NEPSY-II. Early studies on paediatric KTx associated poorer cognitive outcome with early onset of kidney disease [2, 3] and longer disease duration pre-KTx [2]. In more recent studies, however, cognitive impairment has been associated with neurological co-morbidity [1], hypertensive crises and seizures during dialysis [5] and lower socio-economic status [1]. Today, early KTx may alleviate the effects of early onset of kidney disease, yet longer disease duration prior to KTx remains a risk factor for cognitive impairment. Since more demanding patients are accepted for KTx, an increase in neurological co-morbidity may result.

Limitations

The large intra-group age ranges in our study weaken these results. Additionally, we included all patients in the study, even patients with re-Tx and combined liver–kidney Tx. However, we used a comprehensive series of standardized neuropsychological tests designed for a wide age range. All children could be assessed using the same measures, yielding results generalizable across ages. Moreover, we included a healthy control group.

We report more developmental delay and neurological co-morbidity compared to age expectations and to other cohorts of KTx children. However, most of our patients had a congenital disease and received a KTx at a young age. Despite the difficulties of caring for these youngest and smallest patients, their long-term outcomes are quite reassuring. Early KTx with shorter disease duration alleviates later cognitive outcome, while neurological co-morbidity strongly associated with neurocognitive impairment. Poor kidney function at follow-up associated with poorer verbal skills, verbal working memory and complex auditory attention. There seems to be a tendency to under-recognize mental retardation and the need for special education in this patient population. We emphasize the importance of neuropsychological evaluation so that educational needs can be addressed. Children with neurological co-morbidity or longer disease duration are at risk for more general cognitive impairment, yet patients with normal intelligence may also have minor specific neurocognitive deficits and should be evaluated. With correct interventions the children’s learning can be optimized, thereby improving their future schooling and job opportunities and quality of life.

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References


