Internal jugular vein valve incompetence and intracranial venous anatomy in transient global amnesia

S J Schreiber, F Doepp, R Klingebiel, J M Valdueza

Background: Recently a causal relation between internal jugular vein valve incompetence (IJVVI) and transient global amnesia (TGA) has been suggested. IJVVI is postulated to provoke a transient mesiotemporal ischaemia by venous congestion. This mechanism requires a patent venous pathway from the affected IJV through the transverse sinus, confluens, straight sinus (SS), vein of Galen into the basal vein of Rosenthal and the internal cerebral veins.

Objective: To study IJVVI in TGA patients in relation to the intracranial venous anatomy.

Methods: IJVVI was defined if a repeated Valsalva manoeuvre (VM) led to a retrograde jugular flow detected by extracranial duplex ultrasound. Non-contrast venous MR angiography (MRA) was performed to analyse intracranial drainage patterns of the SS in relation to the side of the IJVVI. SS drainage was differentiated into three groups: predominantly right, left, and bilateral drainage. Ultrasound studies were performed in 25 TGA patients and 85 age matched controls. Twenty patients underwent venous MRA.

Results: Sixty eight per cent of patients and 33% of controls showed unilateral or bilateral IJVVI (p = 0.0025). In 36% of patients a TGA preceding VM was reported. Drainage pattern of SS and side of IJVVI corresponded in five of eight patients (63%) with VM and four of 12 patients without VM (33%, p = 0.0994).

Conclusion: Our study confirms the significantly higher prevalence of IJVVI in TGA patients. However, no specific IJVVI related intracranial venous drainage patterns could be found to further support the hypothesis of a direct causal relation between IJVVI and TGA.

Ultrasound protocol

Duplex ultrasound was performed in patients and controls in a head straight, supine position with a 7–11 MHz linear transducer (Powervision 6000, SSA-370A, Toshiba, Tokyo, Japan). IJV b-mode image and Doppler flow were continuously sonated approximately 2 cm above the internal jugular valves using the triplex mode of the ultrasound machine. The Doppler sample volume was set between 0.5 and 1 cm and placed in the centre of the IJV lumen. IJVVI was assessed on both sides after repeated training of the VM.

Abbreviations: IJV, internal jugular vein; IJVVI, internal jugular vein valve incompetence; MIP, maximum intensity projections; MRA, magnetic resonance angiography; SS, straight sinus; TGA, transient global amnesia; TOF, time-of-flight; VM, Valsalva manoeuvre.
subjects during three maximal VMs (duration >5 s). Pictures of the VM were stored on magneto-optical disk. A sufficient VM was confirmed by a clearly visible increase of IJV diameter (approximately 1 cm or more) in the b-mode image. IJVI was concluded if retrograde jugular flow could be seen in the Doppler spectrum during each VM (fig 2). Reduction of flow velocity or zero flow was rated as competent jugular valves.

MRI protocol
Intracranial non-contrast venous MRA was performed in patients only using 1.5 T scanners (Magnetom Vision or Magnetom Symphony, Siemens, Erlangen, Germany). For data acquisition a two dimensional time-of-flight (TOF) MRA protocol was applied (TR 30 ms, TE 6.5 ms, FA 50°, 3 mm slice thickness, 1 excitation 7.19 min, 250 mm FOV, matrix 256 mm). Off-line analysis of the three dimensional MRA data sets was carried out subsequent to data transfer through the intranet on two workstations (SIENET MagicView VB33/Siemens, Germany, and Vitrea/Vital images, USA) using maximum intensity projections (MIP) of about 4 mm slab thickness orientated along the SS axis (fig 3). The SS, confluens, and adjacent horizontal parts of both TS were included in the

Figure 1  Schematic drawing of the venous drainage pathways for the mesiotemporal region (1). The blood drains through the paired basal vein of Rosenthal and internal cerebral veins (2 + 3) into the unpaired vein of Galen and the straight sinus (4 + 5). The straight sinus may drain unilaterally into one or equally into both transverse sinus (7) and from there through the sigmoid sinus (8) into the internal jugular vein (9). (6) Confluens sinuum. (Figure adapted from Feneis H. Anatomische Bildnomenklatur. 2nd edition. Stuttgart: Thieme Verlag, 1970).

Figure 2  Triplex mode ultrasound images of a patient with internal jugular vein valve incompetence in the right jugular vein. Top: resting condition. Doppler spectrum analysis reveals an orthograde continuous flow in the internal jugular vein (IJV). Bottom: image under Valsalva manoeuvre. Note the increased diameter of the IJV (b-mode image, right side) and the temporary reversal of blood flow in the Doppler spectrum.
slab volume. Appearance of the SS drainage side was evaluated by two investigators (RK, SJS) unaware of the presence or side of IJVVI and differentiated into three groups: a predominantly right sided (group A), a predominantly left sided (group B), and a bilateral drainage (group C, fig 3).

Statistical analysis
All presented values are given as means ± standard deviation. Two-sided Fisher’s exact test was performed for comparison of controls and patients. A p value <0.05 was considered significant.

RESULTS

Clinical findings
Twenty six patients were screened; one had to be excluded because of intracranial bilateral high grade stenoses within the carotis-t region. Twenty five patients (9 women, 16 men) aged 61 ± 10 years (range: 37–77 years) and 85 controls (37 women, 48 men) aged 62 ± 9 years (range 48–81 years) were included. The average duration of amnesia in patients was 7 ± 5 hours (range 20 minutes to 18 hours). Nine of 25 patients (36%) had a reliable history of a probable preceding VM (house cleaning and moving of furniture, football play, car mending, fitting a carpet, carrying of flower pots, digging in the garden, sawing wood, skiing, cough attack).

IJV valve incompetence

Ultrasound analysis for IJVVI was performed and evaluated in all controls and patients. IJVVI was found in 28 (33%) controls and in 17 (68%) of TGA patients yielding a significant difference (p = 0.0025). Table 1 illustrates the distribution of right sided, left sided, and bilateral IJVVI, which did not differ between both groups. Two of the eight patients with competent valves (25%) and seven of the 17 with IJVVI (41%, p = 0.66) had a preceding VM.

Venous MRA

MRA was performed in 20 of 25 TGA patients. Analysis of SS anatomy revealed a predominantly right sided drainage in eight (40%), a left sided drainage in five (25%), and a bilateral drainage in seven (35%) cases. Thirteen of the 20 patients did have a IJVVI and eight a preceding VM. The relation of SS drainage and IJVVI sides of patients with and without VM is illustrated in Table 2. IJVVI and SS drainage corresponded in five (63%) of the eight patients with VM and four (33%) of the 12 patients without a reported VM (p = 0.0994).

DISCUSSION

The venous congestion hypothesis for TGA, originally postulated by Lewis in 1998,7 is primarily based on the theoretical consideration that the onset of symptoms often correlates with prior Valsalva-like activities, which may lead to venous reflux through the IJV. IJVVI may be caused by valve insufficiency or aplasia. In anatomical studies, aplasia has been reported to occur in up to 16% of non-selected patients whereas valve competence was not assessed.11 Analysing IJV valve function, three US studies found a significantly higher prevalence of IJVVI in TGA patients, which supports the theory of a causal relation. Sander et al8 analysed the extent of duplex colour inversion during VM whereas Akkawi et al910 used an echo-contrast method evaluating the number of refluxing contrast bubbles in the IJV. Both research groups reported an IJVVI prevalence between 70 and 73% in patients compared with 30 to 47% in controls.8–10 Data of the current study (68% and 33%) confirm this phenomenon and also indirectly validate our chosen duplex US protocol. In addition, the distribution of the affected sides in patients and controls (right/left/bilateral: 68/32/0% and 39/35/6%) appears to be similar to data from Akkawi et al (60/37/3% and 89/0/1%).10 As the high prevalence of right sided IJVVI might correspond to the frequently observed right sided anatomical predominance of IJV drainage,10–11 we additionally performed jugular blood volume flow measurements, which did not yield a correlation between UV flow dominance and the side of the IJVVI (data not shown).

Assuming a causal and not coincidental relation of IJVVI and TGA, two further preconditions must be accomplished to effectively induce a mesiotemporal blood flow disturbance.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Number and distribution of internal jugular vein valve incompetence (IJVVI) in 85 controls and 25 patients</th>
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<tbody>
<tr>
<td>Controls</td>
<td>Patients</td>
</tr>
<tr>
<td>Total IJVVI</td>
<td>28 (100%)</td>
</tr>
<tr>
<td>Right sided IJVVI</td>
<td>19 (68%)</td>
</tr>
<tr>
<td>Left sided IJVVI</td>
<td>9 (32%)</td>
</tr>
<tr>
<td>Bilateral IJVVI</td>
<td>–</td>
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</table>
These are a patent venous pathway and a plausible history of a VM. Concerning the intracranial venous anatomy, the unpaired SS, collecting blood from both mesiotemporal regions through the basal veins of Rosenthal and internal cerebral veins, is a key vessel as its drainage pattern into the confluens can vary considerably." Interestingly, the correspondence of predominant SS drainage and LJVI was slightly but not significantly higher in patients with a VM (63%) compared with those without (33%, p = 0.0994). However, these findings still leave the hypothesis that the TGA in 37% of cases with VM unexplained by the hypothesis. Finally, we could not see any further specific venous morphological characteristics in our TGA patients. Unfortunately, these findings do not deliver further evidence in favour of the venous congestion hypothesis. Yet, they also do not reliably exclude the postulated mechanism as some morphological limitations of our study have to be considered: venous MRA is an increasingly used technique for diagnosis or exclusion of sinus venous thrombosis. However, non-contrast MRA in regions with complex flow patterns might lead to MR signal loss and misinterpretation of venous anatomical variants. Furthermore, the side of the predominant SS drainage might not be as relevant as postulated because intravascular pressure changes can also be transmitted through a non-dominated small or hypoplastic but communicating vessel segment. Also, the postulated functional disturbance might not require a specific morphological correlate as various other pathways of the complex valveless intracranial venous network—for example, the vertebral veins or the paraspinal venous plexus—could as well transmit the venous flow alteration. Finally, the venous reflux do play a role within the aetiology of TGA. Therefore, it is not understood whether aVM, IJVVI, and TGAs should be made towards an even more precise—for example, contrast-enhanced analysis—of the cerebral venous anatomy, including other venous drainage pathways like the vertebral and paraspinal veins. In combination with a functional brain perfusion assessment. Assuming a multifactorial triggering mechanism, other coexisting contributing factors should be considered.

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Competing interests: this study was supported by a grant from the Schering Forschungsgesellschaft mbH, Berlin, Germany.

### REFERENCES


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### Table 2

Distribution of jugular vein valve incompetence (IJVVI) in 20 patients in relation to straight sinus (SS) drainage side (group A–C) and preceding Valsalva manoeuvre (VM)

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>All With VM</td>
<td>All With VM</td>
<td>All With VM</td>
</tr>
<tr>
<td>Right sided UVVI</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Left sided UVVI</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Competent valves</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Group A: right sided SS drainage; Group B: left sided SS drainage; Group C: bilateral SS drainage. Bold numbers indicate plausible constellations according to the hypothesis (left: matching SS drainage and UVVI; right: matching SS drainage and UVVI, including a reported VM).
HISTORICAL NOTE

A note on scrivener’s palsy

For many years—before its recognition as a focal dystonia—writers’ cramp (scrivener’s palsy (from the Latin scribere: to write)) was regarded as an occupational hazard akin to repetitive strain. Lucire in a provocative book suggests that the only new aspect of repetitive strain injury (RSI) is its name.

The first epidemics of writers’ cramp were reported in the 1830s among clerks of the British Civil Service, where it was attributed to the new steel pen nib. Sir Charles Bell gave a description of these disorders:

“...now and then there is a distinct spasm, which cannot be controlled... a disease easily imagined by those who have witnessed the disorder”.

George M Beard who invented the term “neurasthenia” described 125 such cases. In the early 20th century, telegraphists in the UK began experiencing “telegraphist’s cramp”, thought to be caused by the rapid, repetitive movements required to send Morse code, affecting up to 18 per cent of British telegraphists. The suspicion was of a poor constitution, neurosis, and neurasthenic temperament.

Samuel Solly (1805–1871)

Born in London, the son of Isaac Solly and Mary Harrison, Samuel Solly was christened on 13 May 1805 at St Mary Axe. He was educated at Higham Hill Northampton (Disraeli’s school). Solly was apprenticed to Benjamin Travers, a surgeon of St Thomas’ Hospital, and graduated MRCS in 1826. He started in practice at St Mary Axe in 1830.

From 1833–9 he was a lecturer in anatomy and physiology at St Thomas’ Hospital. In 1856 he was elected a Fellow of the Royal Society. He set up practice in 1840 in Savile Row and in 1853 was appointed as surgeon and lecturer at St Thomas’, where he continued until illness forced resignation. He obtained the fellowship in 1843 and later became a council member and examiner at the Royal College of Surgeons of England. His publications included: The Human Brain, its configuration, structure, development, and physiology (London, 1836)—illustrated by references to the nervous system in the lower order of animals; Surgical Experiences (London, 1865)—the substance of clinical lectures; and several of his watercolour pictures were hung at the Royal Academy. A marble bust was presented to St Thomas’ Hospital and the “Solly Prize and Medal” was established in its Medical School in his memory.

He died on 21 September 1871 having fathered 11 children including Richard Harrison Solly who became a Professor of Botany, and Samuel Edwin Solly MD—a chest physician in Colorado Springs where he lived from 1900 having journeyed from England on account of chronic phthisis.

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4 Solly, Samuel (1805–1871) King’s College London College Archives Papers of Samuel Solly, comprising surgical casebook containing notes on patients examined by him at St Thomas’ Hospital, privately, and at Hanwell.

doi: 10.1136/jnnp.2004.044743