Measurement of glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) to predict symptoms of concussion in high-energy trauma

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Background and Rationale

Glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) have been shown to be released in people who have suffered from severe head injuries that show up on brain scans.[12]

These markers have been used as a rule out test for Computerised Tomography (CT) scans in patients presenting with head injuries. However the low specificity 24.9 (95% CI 22.6–27.4)[3] of the test means that they are raised in many patients with a normal CT scan. This same study showed patients with higher biomarker levels had poorer outcomes at 3 months.

Concussion is often underdiagnosed in athletes & the general population,[4]resulting in poor management and prolonged recovery. Undiagnosed concussion could present a danger to athletes participating in sports requiring a high level of concentration such a motorbike racing.

We suspect that patients that have elevated levels of GFAP & UCH-L1 may have a greater incidence of concussion & should undergo screening for a safe return to sport.[5]

Research Questions

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[2] Posti JP, Takala RS, Runtti H, Newcombe VF, Outtrim J, Katila AJ, Frantzén J, Ala-Seppälä H, Coles JP, Hossain MI, Kyllönen A. The levels of glial fibrillary acidic protein and ubiquitin C-terminal hydrolase-L1 during the first week after a traumatic brain injury: correlations with clinical and imaging findings. Neurosurgery. 2016 Sep 1;79(3):456-64.

[3] Lagares A, de la Cruz J, Terrisse H, Mejan O, Pavlov V, Vermorel C, Payen JF, Maignan M, Viglino D, Jacquin L, Douplat M. An automated blood test for glial fibrillary acidic protein (GFAP) and ubiquitin carboxy-terminal hydrolase L1 (UCH-L1) to predict the absence of intracranial lesions on head CT in adult patients with mild traumatic brain injury: BRAINI, a multicentre observational study in Europe. EBioMedicine. 2024 Dec 1;110.

[4] INSIGHTS N. An Underdiagnosed Problem for Athletes?. journal of orthopaedic & sports physical therapy. 2012 Jul;42(7):633.

[5] Martens G, Patricios JS, Schneider KJ, Davis GA, Blauwet C, Feddermann-Demont N, Tooth C, Thibaut A, Kaux JF, Leclerc S. ReFORM synthesis of the 6th International Consensus Statement on Concussion in Sport. British Journal of Sports Medicine. 2025 Jan 23.

Can measurement of glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) predict symptoms of concussion in high energy trauma?

Aims and Objectives

To measure Glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) in patients presenting after a high speed motorcycle crash who require CT head & correlate this with symptoms of concussion using a score derived from the SCAT6 questionnaire.

Study Design and Methods

Study Design

Single centre diagnostic evaluation study

Participants

Will be Competitors in the 2025 Isle of Man TT who are injured during a race or practice session & require a CT scan of their head (Gold standard)

Methods of Measurement

Blood will be taken from the patient as part of their routine treatment or via a finger prick and analysed using the TBI modules of an i-Stat Alinity near patient testing system. (Abotts)

Results of their CT head will be recorded.

Patients will be contacted by researchers at 2 weeks & assessed for concussion symptoms & signs using the 'Symptom evaluation' & 'Cognitive screening' sections of the Sport Concussion Assessment Tool 6 - SCAT6.[6]

https://bjsm.bmj.com/content/bjsports/57/11/622.full.pdf

This will give a score out of 104 with the higher the score being the greater number of symptoms of concussion.

Outcome Measures

Primary – Is raised GFAP & UCH-L1 associated with symptoms of concussion and a higher score using the SCAT6 questions?

Ethical Considerations

Patients with severe head injuries on CT scan will be excluded from the study

[6] Echemendia RJ, Brett BL, Broglio S, Davis GA, Giza CC, Guskiewicz KM, Harmon KG, Herring S, Howell DR, Master CL, McLeod TC. Introducing the sport concussion assessment tool 6 (SCAT6). British Journal of Sports Medicine. 2023 Jun 1;57(11):619-21.

There will be no change in treatment for patients enrolled in the study & those who decline to participate.

All information containing patient identifiable information will be stored securely on Manx care computers or locked folders at Noble's Hospital. The data will only be accessible to appropriately trained members of the research team

Costing

The point of care testing equipment & 30 test modules will be provided by Abbott Point of care testing division as part of a departmental service evaluation for no cost.

Timescales

Due to the time constraints placed by Racing we will plan to start the study on 26th May & complete sample collection by 8th June. We aim to have completed the data collection & processing by mid July 2025 & will put out to publication if suitable in early autumn 2025.

Dissemination

We plan to submit a paper to a suitable Emergency medicine or prehospital care journal.

I would also like to present the findings to the Faculty of Sports Medicine of the Royal College of Surgeons in Ireland.

Copies of any papers will be forwarded to participants & the results shared at Riders meetings & the local Trauma forum.