

Detection of Persisting Concussion Effects on Neuromechanical Responsiveness

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ABSTRACT

WILKERSON, G. B., D. C. NABHAN, C. J. PRUSMACK, and W. J. MOREAU. Detection of Persisting Concussion Effects on Neuromechanical Responsiveness. *Med. Sci. Sports Exerc.*, Vol. 50, No. 9, pp. 1750–1756, 2018. **Purpose:** Assessment of various indices of neuromechanical responsiveness for association with concussion history. **Methods:** An observational cohort study included 48 elite athletes (34 males: 23.8 ± 4.4 yr; 14 females: 25.4 ± 4.5 yr) who performed visuomotor reaction time (VMRT) tests involving rapid manual contact with illuminated target buttons that included two dual-task conditions: 1) simultaneous oral recitation of scrolling text (VMRT+ST) and 2) simultaneous verbal responses to identify the right or left direction indicated by the center arrow of the Eriksen flanker test (VMRT+FT). A whole-body reactive agility (WBRA) test requiring side-shuffle movements in response to visual targets was used to assess reaction time, speed, acceleration, and deceleration. **Results:** Concussion occurrence at 2.0 ± 2.3 yr before testing was reported by 21 athletes. Strong univariable associations were found for VMRT+FT left minus right difference ≥15 ms (odds ratio [OR], 7.14), VMRT+ST outer two-ring to inner three-ring ratio ≥1.28 (OR, 4.58), and WBRA speed asymmetry ≥7.7% (OR, 4.67). A large VMRT+FT by VMRT+ST interaction effect was identified (OR, 25.00). Recursive partitioning identified a three-way VMRT+FT by VMRT+ST by WBRA interaction that had 100% positive predictive value for identification of athletes with concussion history, whereas negative status on all three factors had 90% negative predictive value. **Conclusions:** Performance on dual-task VMRT tests and the WBRA test identified neuromechanical responsiveness deficiencies among elite athletes who reported a history of concussion. **Key Words:** MILD TRAUMATIC BRAIN INJURY, DUAL-TASK CLINICAL ASSESSMENT, NEUROMECHANICS, PERCEPTION-ACTION COUPLING

Sport-related concussion involves mild traumatic brain injury (mTBI) that may elevate risk for long-term neurologic dysfunction. Altered neural processes have been documented to persist for more than three decades after a sport-related concussion (1). At present, advanced neuroimaging and neurophysiologic assessment methods are required to identify subtle abnormalities caused by mTBI that cannot be identified by standard clinical testing methods (2–5). Numerous investigations have documented elevated risk for musculoskeletal (MSK) injury after sport-related concussion (6), which suggests that an unrecognized vulnerability persists beyond the resolution of symptoms and return to sport participation. Unreported cases may contribute to unrecognized abnormalities, as well as evidence that repetitive subconcussive head blows can induce similar subtle effects as those caused by concussion (7). Improved clinical testing methods are

needed to better assess the interrelated neurocognitive and neuromuscular capabilities of athletes who may have elevated susceptibility to MSK injury, and possible risk for long-term alterations in brain function, despite resolution of overt concussion symptoms.

Computerized neurocognitive test batteries are widely used to assess perception, memory, attention, and processing speed, but an important limitation of such testing is lack of substantial engagement of motor processes in the generation of responses to stimuli. Various types of hardware can be used to assess visuomotor reaction time (VMRT), which typically involves manual contact with buttons. Prolonged VMRT has been prospectively associated with MSK injury occurrence among college football players (8). Compared with healthy athletes with no history of concussion, significantly greater differences in VMRT for manual responses to illuminated target buttons located in central versus peripheral visual fields have been documented for athletes with postconcussion visual symptoms (9). Because VMRT testing is typically performed in a static standing position, assessment of whole-body reactive agility (WBRA) may provide more meaningful information about integration of perception-action neural processes that is required during sport participation (10). Virtual reality systems that track body movements in response to visual stimuli may be particularly valuable for such assessment (5,11). The term “neuromechanics” refers to the study of interactions between neural, biomechanical, and environmental

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dynamics (12). We use the term “neuromechanical responsiveness” (NMR) to designate the ability to optimally integrate neurocognitive and neuromuscular processes during participation in sport-related activities. A combination of VMRT and WBRA test results may provide an optimal means to clinically assess the extent to which mTBI has had an adverse effect on NMR.

Dual-task performance creates competition for neural resources that prolongs processing time and requires engagement of executive function to determine the order of neural processing operations (13). Among competing attentional demands imposed by sports, visuospatial processing is clearly crucial for management of environmental interactions. A dual-task that combines a central vision cognitive task with simultaneous engagement of peripheral vision for performance of a VMRT test has been shown to provide greater associations with both concussion history and subsequent MSK injury occurrence than single-task VMRT testing (6). The relative involvement of specific areas within either brain hemisphere, and the degree of interhemispheric communication, depends on the specific demands imposed by a task (14,15). The brain hemispheres differ in terms of specialized neural processing, but functional lateralization is never absolute. The left hemisphere (LH) is considered dominant in >90% of right-handed and >70% of left-handed people (16). The LH is generally dominant for language functions, alphanumeric interpretation, and cognitive abilities (14,17,18), visuomotor control of either hand (14,18), and visuospatial processing of detailed stimuli in both visual fields (19). Thus, a dual task that requires simultaneous verbal recitation of scrolling text (ST) moving across a centrally located screen while using peripheral vision to perform a VMRT test would be expected to impose a relatively greater demand on the LH. The right hemisphere (RH) is responsible for sustained attention and global visuospatial functions in both the right visual field (RVF) and the left visual field (LVF), especially when decision conflict exists (14,20,21).

Decision conflict resolution requires selective attention to a goal stimulus with inhibition of goal distractors, which is adversely affected by mTBI (22). The Eriksen flanker test (FT) is widely used to assess decision conflict created by the incongruent visual display of a set of five adjacent arrows that has a central arrow pointing in a direction opposite to that of two flanker arrows on either side (1,3,20,22,23). Longer processing time is required to respond to central arrow direction for incongruent than congruent (i.e., all arrows pointing in the same direction) displays, which is magnified after mTBI (1,3,22). A meta-analysis of neuroimaging studies demonstrated consistent FT activation of the dorsolateral prefrontal cortex and insula of the RH (19). Thus, a dual task that requires simultaneous verbal responses to FT displays on a centrally located screen while using peripheral vision to perform a VMRT test would be expected to impose a relatively greater demand on the RH (20,23), which would be manifested by slower left-hand responses to stimuli in the LVF.

The efficiency of integrated visual, cognitive, and motor processes can be assessed through dual-task VMRT+ST and VMRT+FT testing, but a more complete representation of an athlete’s capacity for NMR in a competitive sport environment may be derived from a combination of metrics that includes one or more performance indices derived from WBRA testing. The purpose of this exploratory cohort study was to identify a VMRT and WBRA performance profile that would discriminate between athletes who self-reported a prior concussion from those who denied a history of concussion.

METHODS

A cohort of 48 healthy elite athletes (34 males: 23.8 ± 4.4 yr, 178.3 ± 8.9 cm, 80.2 ± 17.5 kg; 14 females: 25.4 ± 4.5 yr, 160.2 ± 27.8 cm, 64.2 ± 12.8 kg) representing six different categories of sport type (Table 1) volunteered to respond to survey questions and participate in NMR tests that were

TABLE 1. Cohort characteristics.

	Concussion History			No Concussion History		
	Male	Female		Male	Female	
<i>N</i>	21			27		
Age (yr)	25.4 (19–34)			23.4 (18–33)		
Sex	13 (62%)	8 (38%)		21 (78%)	6 (22%)	
Sport Type:						
Bobsled/skeleton	3	2		0	2	
Boxing	0	0		6	1	
Figure skating	1	2		3	1	
Gymnastics	2	0		2	0	
Multievent ^a	0	1		5	1	
Wrestling	7	3		5	1	
	Right	Left	Neither	Right	Left	Neither
Hand dominance	20	0	1	21	5	1
≥1 Core or LE injury ^b	86% (18/21)			63% (17/27)		
No. MSK injuries ^c	3.5 (0–11)			1.4 (0–5)		
Sport Fitness Index	53.5 (16–94)			63.3 (24–98)		
DASS ^d	12.0 (0–38)			13.0 (0–37)		

^aMultievent includes modern pentathlon, track & field, triathlon, and weightlifting.

^bCore or lower extremity sprain or strain within previous 12 months (OR, 3.53; 90% CI, 1.05–11.92).

^cMusculoskeletal sprain or strain within previous 12 months (upper extremity, core, or lower extremity).

^dDepression, Anxiety, and Stress Scale.

administered during a single session at a residential training center sports medicine clinic. Written informed consent was obtained from each participant, and all procedures were approved by the institutional review board of the University of Tennessee at Chattanooga. The athletes performed three different 60-s VMRT tests involving rapid manual contact with randomly illuminated buttons on a height-adjustable board (Dynavision D2™ System; Dynavision International, West Chester, OH), and a WBRA test requiring side-shuffle movements in response to 20 randomly presented left or right visual targets (TRAZER® Sports Stimulator; Traq Global Ltd, Westlake, OH). Surveys included the Sport Fitness Index (24), which included an inventory of MSK sprains and strains sustained during the previous 12 months, and the Depression, Anxiety, and Stress Survey (25). Additional survey items acquired information relating to hand dominance, time since last concussion, and total number of concussions sustained in the past.

After a practice trial, each athlete performed a 60-s VMRT test that was limited to manual responses to randomly illuminated buttons. Subsequently, two additional 60-s VMRT tests were performed that involved different dual-task conditions. A centrally located tachistoscope presented ST that the athlete verbally recited while concurrently performing the VMRT test (VMRT+ST). A second dual-task condition displayed the Eriksen FT on the tachistoscope, which required the athlete to verbally indicate the right or left direction indicated by the center arrow of a 20 displays (10 congruent: >>>> or <<<<< and 10 incongruent: >>><> or <<<<<) while concurrently performing the VMRT test (VMRT+FT). The FT arrow sets were displayed for 250 ms, with the interstimulus interval ranging from 2 to 4 s. For each of the three VMRT tests, measures included averaged values for reaction time, outer/inner ratio ($O/I = \text{VMRT for outer two rings} / \text{VMRT for inner three rings}$), and left-right difference ($L-R\text{Diff} = \text{VMRT for left side of board} - \text{VMRT for right side of board}$). The two buttons located immediately above and below the tachistoscope remained inactive during the two dual-task tests (Fig. 1A and 1B).

The WBRA test required the athlete to perform a total of 20 lateral side-shuffling movements in response to the appearance

of virtual reality targets that were randomly displayed on either the right side (10 targets) or left side (10 targets) of a 48 cm × 86 cm monitor (Fig. 1C). A central starting position for the test was 2.7 m from the monitor and a side-shuffling body displacement of 1.8 m was required to deactivate the target, after which the athlete returned to the central position before activation of another right or left target. Whole-body RT was defined as the time elapsed between target appearance and a body core displacement of 17.8 cm in the correct direction. Other measures derived from the virtual reality motion analysis system included averaged values for speed (Spd), acceleration (Acc), and deceleration (Dec), as well as bilateral asymmetry (i.e., percentage difference) of movements performed in opposite directions (RTAsym, SpdAsym, AccAsym, and DecAsym).

Receiver operating characteristic analysis was used to assess the association of each continuous variable with concussion history, and to convert those that demonstrated a prominent cutpoint into binary variables. The odds ratio (OR) derived from cross-tabulation analysis was used to represent the strength of univariable association. A statistically significant association was defined as a 90% confidence interval (CI) lower limit > 1.0 for the OR. Backward stepwise logistic regression analysis was used to identify possible interaction effects among the binary variables, and then to identify the multivariable model that provided the greatest discriminatory power. If two variables demonstrated a significant interaction effect, a single binary interaction variable was created. A 10:1 ratio between criterion-positive cases and the number of variables included in the model was used to avoid model overfitting. Repeated-measures analysis of variance was used to assess left versus right side performance for the dual-task VMRT test results. To assess the possible influence of hand dominance, corresponding analyses for the dual-task VMRT test results were restricted to athletes who reported right-hand dominance.

RESULTS

History of a concussion was reported by 21 of 48 athletes at 2.0 ± 2.3 yr before testing (range, 2 wk to 7.5 yr). Number of previous concussions ranged from 1 to 8, with 33% (7/21)

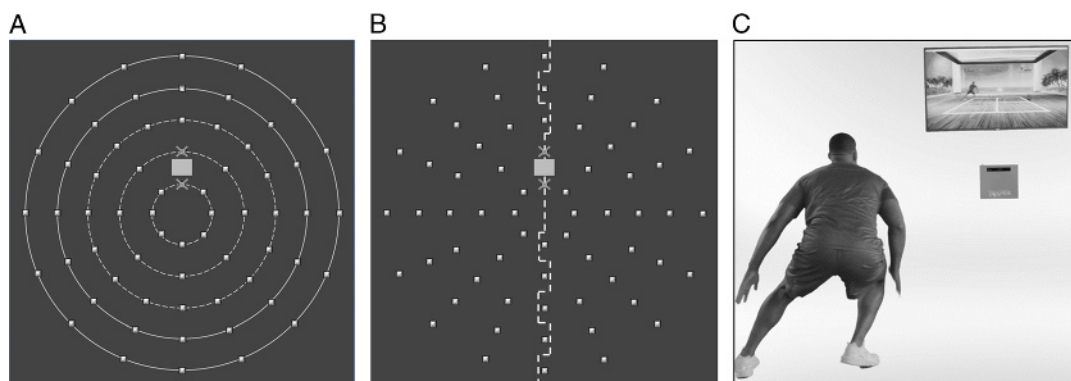


FIGURE 1—Key indices of NMR derived from dual-task VMRT+ST recitation; outer/inner average reaction time ratio (A), dual-task VMRT+Eriksen FT; average left-right reaction time difference (B), and WBRA side-shuffling movement responses to virtual reality visual targets (C).

TABLE 2. Results of univariable and multivariable analyses.

Variable	AUC	Cutpoint	P*	Univariables OR (90% CI)	Four-Factor OR-Adj (90% CI)	Two-Factor A OR-Adj (90% CI)	Two-Factor B OR-Adj (90% CI)
VMRT+FT L-R _{Diff}	0.747	≥15 ms	0.002	7.14 (2.44–20.90)	8.20 (2.28–32.54)	—	—
VMRT+ST O/I	0.675	≥1.28	0.020	4.58 (1.51–13.92)	12.75 (2.19–74.20)	—	—
VMD (Interaction)	—	Both +	<0.001	25.00 (6.00–103.32)	—	41.75 (7.66–227.45)	30.36 (6.27–146.94)
WBRA Acc _{Asym}	0.651	≥2.5%	0.052	4.75 (1.18–19.17)	5.82 (0.98–34.58)	—	—
WBRA Spd _{Asym}	0.633	≥7.7%	0.014	4.67 (1.63–13.36)	16.36 (2.74–97.79)	9.41 (2.09–42.43)	—
RMA (interaction)	—	Both +	0.007	6.33 (2.01–19.87)	—	—	8.39 (1.96–35.96)

*Fishers exact test one-sided P value.

AUC, area under curve, receiver operating characteristic analysis; OR-Adj, adjusted OR derived from logistic regression analysis of binary variables; VMRT+FT L-R_{Diff}, dual-task VMRT+FT, average reaction time, left minus right difference; VMRT+ST O/I, dual-task VMRT+ST, average reaction time, outer two rings divided by inner three rings; VMD, both VMRT+FT L-R_{Diff} ≥ 15 ms and VMRT+ST O/I ≥ 1.28; WBRA Acc_{Asym}, Whole-body reactive agility acceleration asymmetry; WBRA Spd_{Asym}, Whole-body reactive agility speed asymmetry; RMA, reactive movement asymmetry, both WBRA Acc_{Asym} ≥ 2.5% and WBRA Spd_{Asym} ≥ 7.7%.

reporting a single concussion and 67% (14/21) reporting multiple concussions. Concussion occurrence within the previous 12 months was reported by 52% (11/21). Univariable analysis results for each variable that demonstrated receiver operating characteristic area under curve > 0.60 and OR > 2.0, as well as multivariable logistic regression results, are presented in Table 2. Strong univariable associations were found for VMRT+FT L-R_{Diff} ≥ 15 ms (OR, 7.14; 90% CI, 2.44–20.90), VMRT+ST O/I ≥ 1.28 (OR, 4.58; 90% CI, 1.51–13.92), and WBRA Spd_{Asym} ≥ 7.7% (OR, 4.67; 90% CI: 1.63–13.36). A strong VMRT+FT by VMRT+ST interaction effect was identified (OR, 25.00; 90% CI, 6.00–103.32), which we designated as visuomotor dysfunction (VMD). An interaction effect was also identified between WBRA Spd_{Asym} and WBRA Acc_{Asym}, which we designated reactive movement asymmetry. Analyses for assessment of the possible influences of time since last concussion and number of previous concussions failed to demonstrate any significant effects.

The strongest two-factor model included VMD (suboptimal performance on both dual-task VMRT tests) and WBRA Spd_{Asym} ≥ 7.7% (model χ^2 , 27.46; $P < 0.001$; Hosmer & Lemeshow Goodness of Fit χ^2 , 0.24; $P = 0.89$; Nagelkerke $R^2 = 584$). The VMD factor had 88% positive predictive value (14/16) and 78% negative predictive value (25/32). Recursive partitioning revealed that the combination of suboptimal

VMD and WBRA Spd_{Asym} ≥ 7.7% had 100% positive predictive value for identification of athletes with concussion history, whereas negative status on both factors provided 90% negative predictive value (Fig. 2).

For VMRT+ST, both groups of athletes demonstrated significantly faster performance on the left side than the right side (Fig. 3A; Side main effect: $F_{1,46} = 3.78$; $P = 0.058$). For VMRT+FT, a significant interaction was evident (Fig. 3B; group side effect: $F_{1,46} = 8.35$; $P = 0.006$). Analyses restricted to athletes who reported right-hand dominance (41/48; 20 with concussion history and 21 with no concussion history) demonstrated similar results for both VMRT (Fig. 3C; side main effect: $F_{1,39} = 9.88$; $P = 0.003$) and VMRT+FT (Fig. 3D; group side effect: $F_{1,39} = 6.61$; $P = 0.014$).

DISCUSSION

Altered functional connectivity between spatially separated brain areas after concussion has been documented among individuals with normal clinical test results (3,26,27). Hypoconnectivity of a brain network can result from diffuse axonal injury within white matter tracts, whereas hyperconnectivity appears to be a compensatory response that increases utilization of neural resources as a means to sustain normal cognitive functions

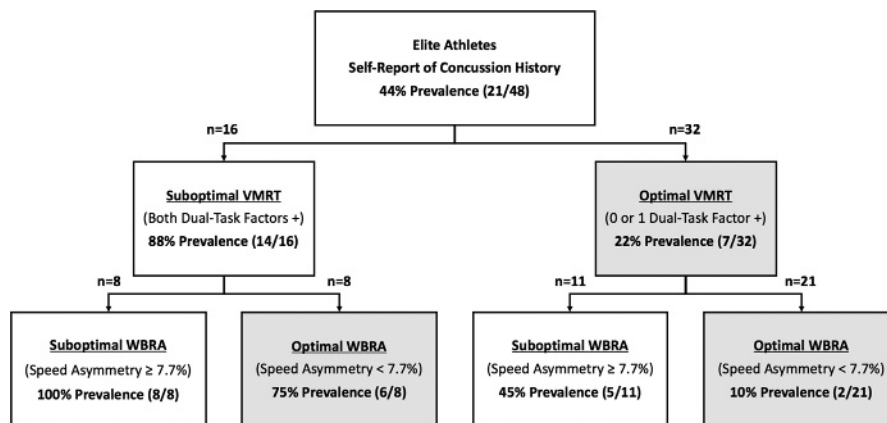


FIGURE 2—Classification tree for dual-task visuomotor performance interaction factor combined with WBRA side-shuffle speed asymmetry factor. First-level partitioning on the basis of visuomotor dysfunction (below cut-point for both VMRT dual-task tests vs below cutpoint for only one or neither of the tests) demonstrated a fourfold difference in concussion prevalence (88% vs 22%), which corresponds to 88% positive predictive value and 78% negative predictive value. Second-level partitioning on the basis of suboptimal WBRA speed asymmetry demonstrated a tenfold difference in concussion prevalence for cases positive at both levels vs negative at both levels (100% vs 10%), which corresponds to 100% positive predictive value and 90% negative predictive value.

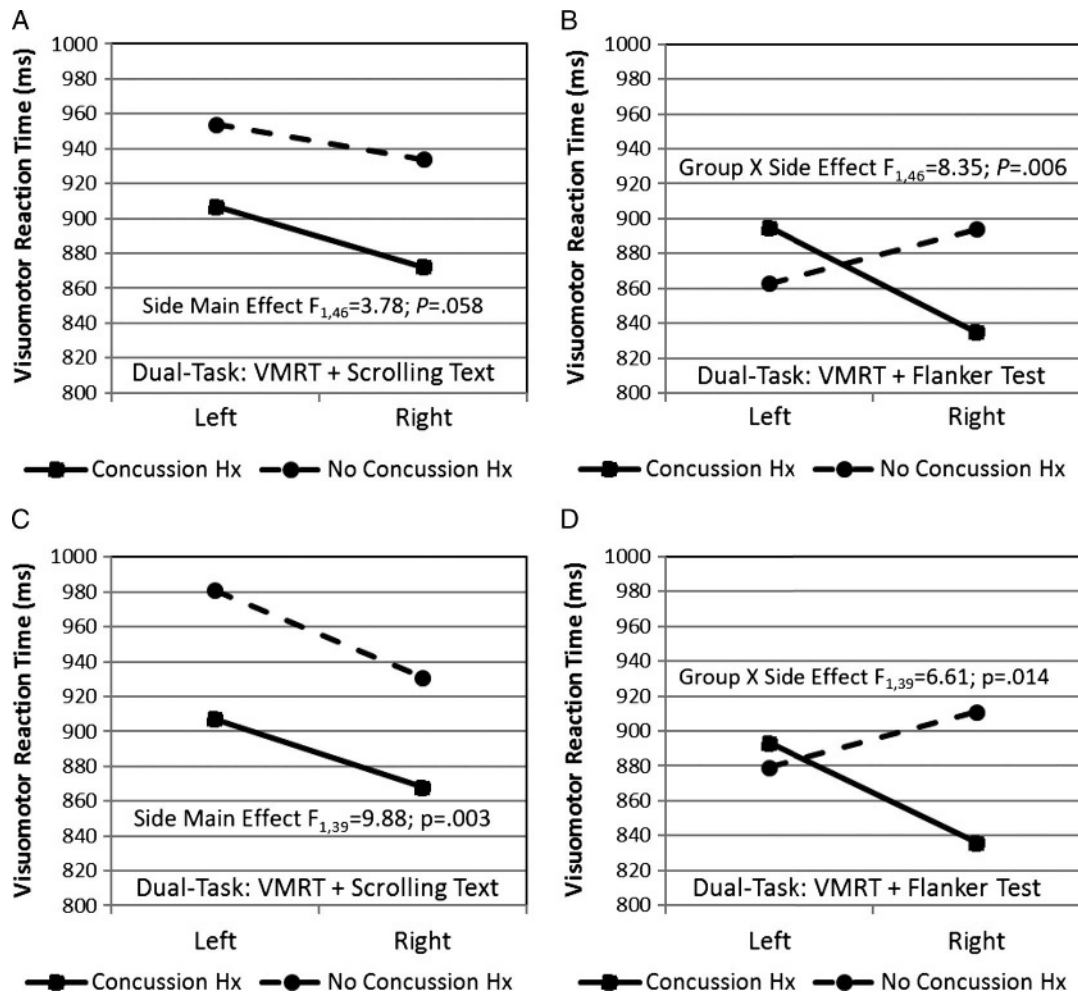


FIGURE 3—Follow-up comparative analyses of the dual-task VMRT tests. Entire cohort ($n = 48$), left side vs right side VMRT differences for the ST test (A) and the Eriksen FT (B). Analysis limited to right-handed athletes ($n = 41$), left side vs right side VMRT differences for the ST test (C) and the Eriksen FT (D).

(4,26–28). Although hyperconnectivity can maintain the ability to perform executive functions, the costs are manifested by cognitive fatigue and slowed neural processing (27,28). Dual-task assessment appears to be essential for detection of subtle neuromechanical abnormalities, which are revealed through overload of neural processing resources (13,29,30).

Task specificity. Flanker test performance relies on visuospatial processing that imposes greater demands on the RH than the LH, with incongruent FT stimuli eliciting the greatest activation level (20,23). Our finding of a strong association between VMRT+FT L-RDiff ≥ 15 ms and concussion history is consistent with abundant evidence supporting RH specialization for the interrelated neural functions underlying sustained attention, visuospatial processing, and conflict resolution (2,15,17,18,20,21,23,31–35). The relative influences of hand dominance, eye dominance, lateralized brain functions, and the need for interhemispheric transmission of neural information on manual reaction time depend heavily on the specific nature of the task design (18,21,36–39). When a single-task VMRT light stimulus and the response hand are on the same side, the contralateral hemisphere directly receives the

visual input and initiates the motor response without the necessity for interhemispheric communication (36,37). Because the RH receives input directly from the LVF and directly controls the left hand motor response, our finding of faster left side VMRT+FT responses for healthy individuals might be expected (21). If the RH is overloaded during the performance of a task that requires both visuospatial processing and sustained attention, a slowed response to a visual stimulus in the LVF may be observed (18,21). Transcranial magnetic stimulation of the RH parietal lobe to temporarily disrupt normal function has been shown to impair visuospatial judgment in the LVF, whereas stimulation of the LH had no effect (35). Therefore, a strong theoretical explanation exists to support our finding of relatively slower VMRT+FT responses in the LVF among athletes with a concussion history.

Both groups exhibited faster RVF than LVF responses for the VMRT+ST test, which may be explained by direct RVF input and control of the right hand by the LH, along with a lack of a dual-task overload effect on LH function. Engagement of the LH for word recognition and verbal recitation is relatively automatic process that may impose little or no incremental

demand for neural resource allocation (15). Because the efficiency of lateralized brain processing may differ on the basis of hand dominance (38), a follow-up analysis of the VMRT+ST data that was restricted to right-hand dominant athletes demonstrated a stronger RVF performance advantage than the finding for the entire cohort of athletes. Although the dual-task VMRT+ST test did not demonstrate a side-specific VMRT association with concussion history, the ratio of peripheral response speed (i.e., targets located at a viewing angle $\geq 45^\circ$) to central response speed (i.e., targets located at a viewing angle $< 45^\circ$) was found to have discriminatory value. Consistent with previously reported findings from preliminary studies (6), VMRT+ST O/I appears to be a sensitive indicator of a persisting concussion effect. Both VMRT+FT L-RDiff and VMRT+ST O/I appear to provide unique information, but discriminatory power was significantly increased when the two test results were combined as a single VMD variable. Thus, two different dual-task VMRT tests are needed for optimal identification of persistent visuomotor dysfunction among athletes with concussion history. Our analysis demonstrated that the WBRA test contributed unique information to the multivariable model, which is consistent with previous reports that whole-body engagement can identify a lingering concussion effect referred to as perceptual-motor disintegration (5,11). A potentially important aspect of whole-body engagement is activation of the cerebellum, which is believed to play a critical role in generation of motor responses to sensory input (26,29). Diffuse axon injury in the genu of the corpus callosum, the right anterior corona radiata, and the left superior cerebellar peduncle may be responsible for disruption of normal connectivity between the right prefrontal cortex and the left cerebellum (2,31).

Limitations. A potentially important limitation of the dual-task VMRT tests is lack of whole-body engagement. Perception-action coupling is a dynamic process that involves brain, body, and environmental interrelationships that may not be adequately represented by finger micro-movements (e.g., mouse-click responses) or relatively isolated upper extremity movements (10). A limitation of our WBRA test was lack of a concurrent cognitive demand on the frontoparietal attention network, which might have provided greater evidence of perceptual-motor disintegration (40). Bi-directional whole-body responses to the appearance of simple visual targets probably presented a lesser challenge to available neural processing resources than more complex visual stimuli that require cognitive interpretation, such as the incongruent FT visual stimuli.

Reliance on self-report of concussion history is clearly a limitation, but underreporting would not be expected to

produce an overestimation of the observed associations with indices of NMR. Definitive evidence of a link between microstructural damage within specific white matter tracts with NMR deficiencies will require acquisition of both neuroimaging and clinical test data for each athlete included in the study. Other limitations of this study include the heterogeneous representation of sports that impose differing physical demands and too few female athletes to assess differential associations between sexes. Future studies need to analyze larger datasets that are specific to sport and sex, which will be necessary to develop population-specific standards for optimal clinical test performance. Associations of concussion history and NMR measures with core or lower extremity sprain or strain occurrence within the previous year will be addressed in a future report. Further research is also needed to prospectively assess the association of NMR performance values with MSK injury incidence rate within a specified surveillance period, and to assess the effectiveness of targeted interventions for improved function and injury risk reduction.

CONCLUSIONS

Neural processing limitations and inefficient compensatory functional connectivity may be objectively identified through specific clinical testing procedures that are designed to identify suboptimal NMR, which may explain elevation of MSK injury risk after concussion. Clinical testing that identifies differential visuospatial response speed between visual hemifields, impaired responsiveness to peripheral visual stimuli, or asymmetrical whole-body movement capabilities can be done with commercially available systems, which provide a feasible means to acquire data that appear to be highly relevant individualized concussion management.

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