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Davies, David James; Yakoub, Kamal; Su, Zhangjie; Clancy, Michael; Forcione, Mario; Lucas, Sam; Dehghani, Hamid; Belli, Antonio

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The Valsalva maneuver: an indispensable physiological tool to differentiate intra versus extracranial near-infrared signal

DAVID JAMES DAVIES,[1,2,3,6] KAMAL MAKRAM YAKOUB,[1,2,3,6,*] ZHANGJIE SU,[1,3] MICHAEL CLANCY,[4] MARIO FORCIONE,[3] SAMUEL JOHN EDWIN LUCAS,[5] HAMID DEHGHANI,[4] AND ANTONIO BELLI[1,2,3]

[1]*National Institute for Health Research Surgical Reconstruction and Microbiology Research Centre (NIHR SRMRC), University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK*
[2]*Department of Neurosurgery, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK*
[3]*Neurotrauma and Ophthalmology Research Group, Institute of Inflammation and Aging, University of Birmingham, Birmingham, UK*
[4]*School of Computer Science, University of Birmingham, Birmingham, UK*
[5]*School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, UK*
[6]*Co-first authors with equal contribution*
[*]*k.yakoub@bham.ac.uk*

Abstract: Developing near-infrared spectroscopy (NIRS) parameter recovery techniques to more specifically resolve brain physiology from that of the overlying tissue is an important part of improving the clinical utility of the technology. The Valsalva maneuver (VM) involves forced expiration against a closed glottis causing widespread venous congestion within the context of a fall in cardiac output. Due to the specific anatomical confines and metabolic demands of the brain we believe a properly executed VM has the ability to separate haemodynamic activity of brain tissue from that of the overlying scalp as observed by NIRS, and confirmed by functional magnetic resonance imaging (fMRI). Healthy individuals performed a series of standing maximum effort VMs under separate observation by frequency domain near-infrared spectroscopy (FD-NIRS) and fMRI. Nine individuals completed the clinical protocol (6 males, age 21-40). During the VMs, brain and extracranial tissue targeted signal were significantly different (opposite direction of change) in both fMRI and NIRS ($p=0.00025$ and 0.00115 respectively), with robust cross correlation of parameters between modalities. Four of these individuals performed further VMs after infiltrating 2% xylocaine/1:100,000 epinephrine (vasoconstrictor) into scalp tissue beneath the probes. No significant difference in the cerebrally derived parameters was observed. The maximum effort VM has the ability to separate NIRS observable physiology of the brain from the overlying extracranial tissue. Observations made by this FD cerebral NIRS device are comparable with fMRI in this context.

1. Introduction

Since its clinical introduction cerebral near-infrared spectroscopy (NIRS) has developed into an attractive method of monitoring brain tissue in a variety of clinical contexts. The development of NIRS parameter recovery techniques and its related hardware is progressively evolving. This expands its potential utility into an ever wider range of clinical and scientific disciplines [1]. Within certain contexts improvements to inter- subject variability; more reliable absolute chromophore concentration measurement and reduction in extracranial tissue (ECT) influence on parameters are critically important. Frequency domain [1–2], time domain [3], and contrast

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enhancement [4], represent just some of the avenues of research and system development at the forefront of this technology (Fig. 1).

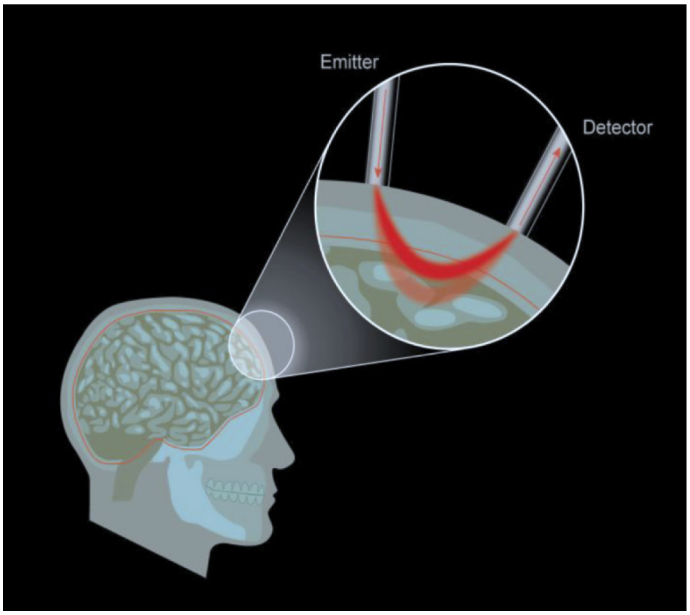

Fig. 1. NIRS concept illustrated.

Within any context, validating the origin of recovered cerebral NIRS parameters can prove challenging. Confirmation that the parameters recovered are specifically reflective of changes in the brain may be useful. The influence of overlying ECT and its rich blood supply on brain targeted NIRS recovered parameters is one of the principle challenges of NIRS technology development. This is also true within the clinical setting, when NIRS is being introduced as a cerebral monitoring modality. In such cases a simple and reproducible physiological manoeuvre that could clearly separate the morphology of haemodynamic activity of extracranial and intracranial tissues would be extremely useful.

The Valsalva maneuver (VM) involves forced expiration against a closed glottis, leading to a subsequent increase in intrathoracic pressure thus impeding return from the venous circulation to the right atrium (Fig. 2). Congestion within the intracranial venous vasculature due to this then causes a rise in intracranial pressure (ICP). A fall in arterial blood pressure then ensues due to a reduction in circulatory return, which leads to a compounding reduction in cerebral perfusion.

The VM is therefore a useful method of simulating a rise in intracranial pressure with both reduced perfusion and venous congestion [5]. It was originally devised as a method of demonstrating tympanic membrane integrity in 1704 by Antonio Valsalva, an Italian physiologist and scientist. The technique is easily performed consistently with appropriate monitoring of end-tidal gas composition to monitor respiratory frequency, and beat-to-beat blood pressure to ensure adequate intrathoracic pressure is achieved.

Importantly, the VM may be useful in the validation of NIRS parameter origins as it induces a theoretical separation in physiological activity (on demand) between the superficial ECT and the underlying brain [6]. Specifically, during the Valsalva the skin and ECT experience venous congestion and a pooling of blood within their capillary network. We hypothesised that as their metabolic demand during the resting state is theoretically negligible [7], the relative saturation of the tissue remains consistent or marginally increases during the significant capillary blood volume increase during VM. Conversely during the same period within the confines of the skull,

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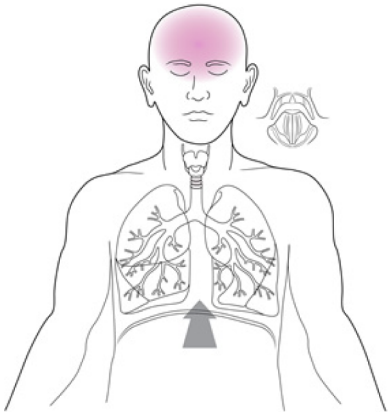

Fig. 2. Principles of the Valsalva maneuver. Forced expiration against a closed glottis, with pooling of the venous blood due to raised central venous pressure.

volumes are fixed. Therefore this venous conjunction leads to an increase in intracranial pressure and reduced cerebral perfusion. This is then compounded by a fall in blood pressure, with the brain's considerable metabolic demands (stripping out the oxygen from the static pooled vasculature) leading to a relative decrease in tissue haemoglobin saturation [8].

Functional magnetic resonance imaging (fMRI) is a useful method of monitoring cerebral activity in both a resting or stimulated state. Chiefly, fMRI utilises Blood Oxygen Level Dependant contrast (BOLD) to anatomically resolve activity within the brain. The BOLD contrast method was developed by Ogawa et al, and has been adopted as a method of mapping cortical activity and cerebral function [9]. The technique is able to identify changes in the relative quantity/proportions of deoxygenated haemoglobin within a specified region of interest (ROI) or voxel. Oxygenated blood is largely diamagnetic (net nil effect) whereas deoxygenated blood is largely paramagnetic and differing relative quantities of each lead to detectable inhomogeneity in the MR signal.

Neurological tissue has no inherent energy or oxygen donating stores. Therefore the supply of these is entirely blood flow dependant. A given increase in neurological function/work done within a ROI will facilitate an increase in blood flow (fundamental neurovascular coupling). The specific character and duration of the neurological activity within this region will then influence the remaining relative proportions of oxygenated and deoxygenated haemoglobin. This basic principle underpins the extrapolation of MR BOLD data to be interpreted as cerebral tissue function (Fig. 3).

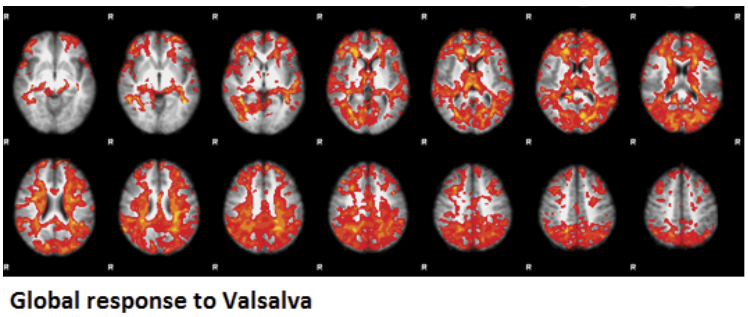

Fig. 3. fMRI/BOLD response to stimulus. BOLD signal during peak Valsalva intensity, brighter areas denoting higher relative concentrations of deoxyhaemoglobin.

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As NIRS-based parameters detect relative proportions of their key chromophores oxygenated and deoxygenated haemoglobin, the use of BOLD contrast signal as a yardstick or 'gold standard' for the validation of NIRS is frequently adopted [10]. BOLD signal is indicative of relative change (with output parameters in arbitrary units). Values for absolute metabolic delivery and demand are not readily derivable, only the magnitude and timing of changes can be compared with NIRS parameters.

As previously discussed, the influence of the extracranial tissue component of recovered NIRS parameters is an important factor needing quantification. A measurable reduction in skin perfusion and the subsequent effect on any observation of cerebral activity could provide valuable insight into the extent to which these tissues actually mask physiological changes (within the context of the VM).

2. Aims

We aim to assess the observations made by NIRS in both cerebral (frontally placed) and extracranial tissues (zygomatic facial skeleton) during a series of maximal exertion VMs in healthy individuals. We hypothesised that during a maximum effort Valsalva changes in tissue perfusion activity may differ markedly between the extracranial tissue and the brain as previously discussed.

We compared the NIRS derived data to that obtained from fMRI- BOLD of the corresponding cerebral and extracranial regions during the same maneuvers (in the same individuals under identical conditions).

From here a vasoconstrictive agent (a mixture of local anaesthetic and epinephrine, 2% xylocaine/1:100,000 epinephrine) was injected into the skin underlying the NIRS optodes and the influence of reducing blood flow on the recovered parameters was investigated.

3. Materials and methods

3.1. Participants

Nine healthy volunteers (6 males, age 21-40) were prospectively recruited to take part in this study after providing their informed written consent. Ethical approval was obtained by the University of Birmingham Research Ethics Board (Ref.: ERN_30-1031) conforming to the Declaration of Helsinki.

3.2. Equipment

A frequency domain NIRS (FD-NIRS) device (OptiplexTS™, ISS Inc. Illinois USA) was used to obtain our NIRS-based parameters. In standard form, this device utilises a single NIR light detector with 4 individual sources at 30, 35, 40 and 45mm distances (each emitting the 2 device standard wavelengths of 680 and 830nm). This configuration broadly allows for parameters to be recovered (at useful resolution) from approximately 22.5mm below the surface (target depth). A principle advantage of FD-NIRS over more conventional continuous wave NIRS devices (utilised in the vast majority of clinical trials) is that values for light scatter within the tissues are not simply assumed. The intensity of the emitted light is modulated and the shift in phase quantified, theoretically allowing for characterisation of the specific coefficient of scatter (rather the reliance of a fixed assumed value in continuous wave devices) and closer absolute values of chromophores to be derived. The relative chromophore concentrations, and from these the saturation (the output parameter considered by this investigation) are calculated using the established [11] multi-distance approach, incorporating phase shift measurements at the respective source/detector distances to provide a tissue specific value for the coefficient of scatter (μ's). This value is then re-incorporated into a modified Beer-Lambert formulation.

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For the acquisition of brain-derived NIRS data, the same location for optodes on the forehead surface was selected in all participants. Right and left probes were placed 3cm above the superior orbital ridge on the forehead (below the hairline), with the lateral border of the pads approximately 5mm medial to the superior temporal line (to minimise muscle activity interference). This equated to a NIRS field of acquisition approximately incorporating the middle frontal Gyrus (Brodmann area 10).

Data from extracranial tissue was obtained by repeating the protocol with probes directed at a specific site on the facial skeleton (Fig. 4). As this device was being used in an 'as purchased' form, source detector distances were not modified and post hoc manipulation of the raw device output data was not undertaken. Optimisation of optode probe location was selected to capture data from somatic tissue (avoiding contamination from neurological tissue or disruption from air cavities/sinuses). Optodes were therefore placed along the line of the zygomatic arch, incorporating only skin, zygomatic bone and pterygoid muscle tissue within a 2.5cm depth (beyond target depth of the device). Ideally parameters would be recovered from the superficial tissue overlying the forehead (identical location to the site of brain signal acquisition); however, without modification superficial tissue signal cannot reliably be isolated with this device. Physiologically the difference in location suggested for signal acquisition should make no difference to the results seen, as they are not only within close proximity but also supplied by identical sources and have similar neuronal innervation.

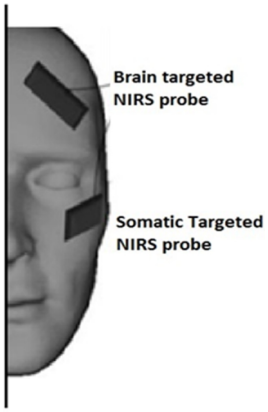

Fig. 4. Placement of NIRS probes for brain and non-brain (somatic tissue) examination.

For the purposes of this investigation tissue saturation (relative ratio of oxygenated/total haemoglobin) was utilised as a sole NIRS parameter, as direct quantitative comparisons for each chromophore are not possible with the fMRI data. As briefly described, the paramagnetic influence of the deoxygenated haemoglobin is the more influential component of the supplied blood on the BOLD parameters. As a constituent, its increasing concentration leads to a reduction in the signal providing a plausible parallel to the NIRS observed 'desaturation'.

A Phillips Achiva 3T MRI scanner was used to acquire fMRI data. Following basic structural T1 images for anatomical reference, a single shot echo-planar imaging (EPI) sequence using a 32 channel coil was obtained during VM. For each sequence a 3×3x3mm voxel size was employed with no slice gap (ascending acquisition). The flip angle in this sequence was 80 degrees with an echo time of 30ms and a repetition time of 2ms. Separate sequences were acquired from each VM, with instructions relayed to participants via a customised (Matlab code based) visual feedback system. After normalisation into standard Talairach space the single voxel region of interest was positioned in each case in a similar position to the NIRS acquisition region over the white/grey matter junction of the middle frontal gyrus (Brodmann area 10) bilaterally as stated

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above. Here output data from each side was combined into a single data stream (utilising the structural T1 images). Extracranial BOLD signal was derived by free hand placement of each voxel into an area of facial somatic tissue corresponding with the field of acquisition of the NIRS probes at their described point of placement; and again a bilateral average formulated a single output data stream. Care was taken to place the region of interest within vascular hypodermal tissue, avoiding frankly avascular structures such as cortical bone, fat or the superficial dermis.

3.3. Procedure

Equipment compatibility did not permit contemporaneous NIRS and fMRI observation. Therefore the test protocol was executed separately with each modality under similar conditions, but temporally distinct.

Participants completed a protocol incorporating supine maximal exertion VMs with periods of complete rest while under observation by both NIRS and fMRI. Separate identical clinical protocols were performed on each participant. In both cases the adequacy and duration of VM were monitored via end-tidal carbon dioxide partial pressure measurement (PetCO2), finger photoplethysmography (Portapres, Finapres Medical Systems, The Netherlands) allowing accurate real-time monitoring of blood pressure. Absolute values for blood pressure were not incorporated into the data set; the key focus was on maintaining consistency in the morphological response to VM only.

During fMRI PetCO2 was monitored using a modified non-return face mask and respiratory gas probe. Participating individuals were then requested to perform a maximal effort VM. We aimed to induce the classical four phase blood pressure response [12], the presence of which enabled us to ensure consistency.

In order to produce consistent photoplethysmography signature VMs with as little movement and material artefact as possible, a series of pre-test rehearsals were carried out. To produce the most reproducible and clear haemodynamic VM signatures a maximal effort maneuver had been selected. This also negates the need for a complex external exhalation pressure regulator.

NIRS and fMRI testing were performed immediately after one another in each individual, a minimum 10 minute period of rest was required to ensure baseline PetCO2 levels were restored (as PetCO2 can significantly influence the Valsalva response) [13].

Event logging was synchronised between modalities during the protocol in a mode similar to those previously employed in the literature demonstrating that the changes in physiology induced are detectable by NIRS devices [14–17].

3.4. Analysis

BOLD data (Arbitrary Units) was acquired from each specified region of interest (ROI) at a rate of 1Hz and matched contemporaneously with NIRS data (saturation %) acquired at the same frequency.

Analysis of the net change in parameters during Valsalva was done utilising the Wilcoxon rank sum method with multiple pairwise comparisons between the brain and ECT signals for both modalities. Time series and cross correlative statistical analysis were also undertaken.

To normalise the output data, the initial parameter value (at 1 second) was subtracted from all values thereafter. These were then scaled by the largest absolute value. This was repeated for each participant so that all scaled values lie in the range -1 to 1.

The distribution and scaled values over time for each group were then modelled incorporating non-linear spline functions for the effect of time. The Welch–Satterthwaite equation was employed to investigate baseline pooled variance (prior to VM), this confirmed that at the time of observation no difference in scaled values (all data normalised) between the NIRS and fMRI values from both brain and ECT was present. The Kolmogorov-Smirnov test (two sample) was then employed to analyse the temporally based changes (during VM) as two continuous one

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dimensional data streams (brain and ECT). This test is primarily used to determine if continuous streams of data are likely to originate from the same source.

The cross-correlation function (CCF) of the two univariate samples was then considered, allowing causality between modalities to be assessed using a Granger test (e.g. Examining NIRS parameters at a given time, and how does that predict simultaneous fMRI parameters incorporating the derived value for lag).

3.5. Reduction in skin perfusion

Participants then underwent infiltration of the forehead tissue (skin/scalp) directly underneath the applied cerebrally directed NIRS probes with a mixture of vasoconstrictor and local anaesthetic agent. This was undertaken after their initial NIRS VM protocol had been completed. Here 2 mL of 2% xylocaine with 1:100,000 epinephrine was infiltrated into the forehead skin. Probes were then applied after the capillary refill time at the area of infiltration exceeded 4 seconds. Skin perfusion pre- and post-application of the xylocaine with epinephrine was formally confirmed using laser-Doppler (DRT4, Moor Instruments Ltd, UK) to accurately quantify the effects of the vasoconstrictive agent. This participant then repeated the VM protocol.

4. Results

4.1. Changes during Valsalva

In all cases a satisfactory consistency in both the effort and timing of VM was achieved. Each measurement was not considered separately, but processed as a total average reading (peak value) across all subjects and both sides of the head. During VM, both fMRI and NIRS output parameters showed a decrease in saturation (compared to the average value of the baseline) for brain targeted approaches, while ECT targeted approaches showed an increase. Specifically, prefrontal NIRS saturation decreased by 7.2% (S.D 4.77%) and fMRI decreased by 3.4% (S.D 1.46%) from baseline, whereas ECT NIRS increased by 6.1% (S.D 2.72%) and fMRI increased by 4.4% (S.D 3.45%). These brain and ECT signals were found to be significantly different in both fMRI and NIRS ($p = 0.00025$ and 0.00115 respectively). Each individual performed only 1 VM within the MRI scanner (9 VMs) and a series of 2 VMs (18 VMs) while under NIRS observation. This demonstrates the ability of both modalities in this instance to differentiate brain from ECT during shifts in intracranial physiology. It also confirms that both modalities support our initial hypothesis relating to the separation of haemodynamic physiology between brain and superficial tissues (Fig. 5).

4.2. Agreements between modalities

Visual inspection indicated that both modalities have good agreement in their changes over time. Kolmogorov-Smirnov analysis demonstrated that the bilateral brain-derived NIRS parameters and fMRI BOLD data from the bilateral middle frontal gyrus (MFG) unlikely to be from different sources ($p = 0.275$) (Fig. 6).

We found that the greatest CCF between modalities of 0.613 occurs when the fMRI BOLD brain values are lagged by 0.5 seconds. Granger analysis based on the value for data lag derived suggests that NIRS brain values are associated with fMRI BOLD brain values ($P = 0.05$).

Similar analysis was then undertaken of the ECT parameters recovered from both NIRS and fMRI during VM. Once again on visual inspection of the data demonstrated that each modality displays general agreement, although the specific morphology of the wave does not appear to have the same degree of conformity to the brain derived data (Fig. 7). On applying the Kolmogorov-Smirnov test on these data we obtain a p-value of <0.001, suggesting that we have strong evidence in the data to indicate that these samples come from different distributions (as may be predicted by the visual differences observable, not seen in the brain derived data). With

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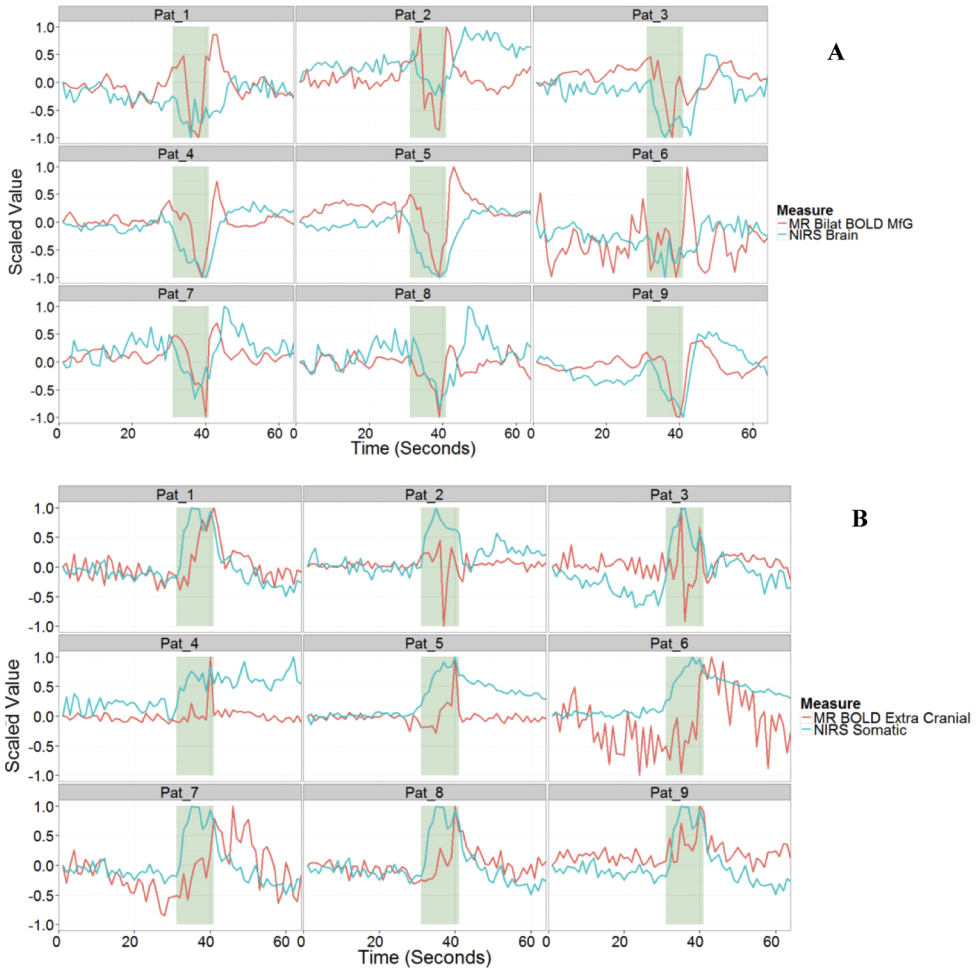

Fig. 5. NIRS vs fMRI BOLD individual patient data streams during Valsalva. A) NIRS vs fMRI BOLD brain derived Valsalva signals. B) NIRS vs fMRI BOLD extracranial derived Valsalva signals

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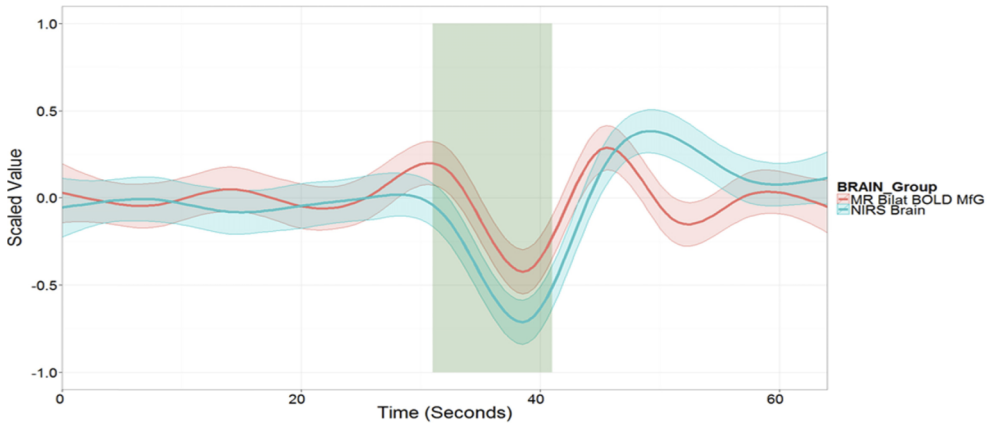

Fig. 6. NIRS vs fMRI BOLD brain derived Valsalva signal; a net reduction in parameters detected by both modalities.

regard to predicting activity between modalities; the greatest CCF occurs at 5 seconds (lag) and applying this to the Granger model with a switched direction of causality suggests that NIRS brain values are associated (strong cross correlation) with fMRI BOLD brain values ($p = 0.5$).

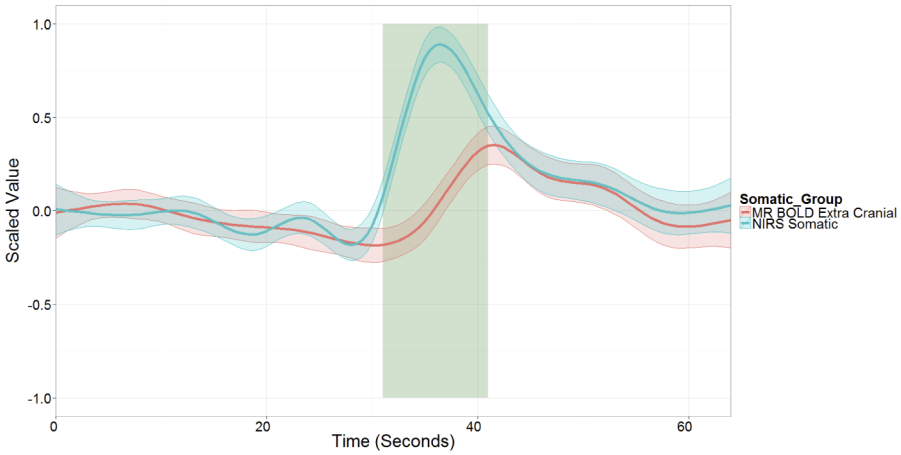

Fig. 7. NIRS vs fMRI BOLD extracranial derived Valsalva signal; a net increase in parameters detected by both modalities. Measurements from all subjects and bilaterally formed into a single data stream. Tissues overlying Brodmann area 10/MFG selected as the region of interest.

4.3. Reducing perfusion to the superficial tissues

Of the original participants ($n = 9$), four individuals agreed (not additional individuals) to perform a further series of 17 VMs after the infiltration of xylocaine/epinephrine into the cutaneous and subcutaneous tissues at the prefrontal site beneath the NIRS probes (brain targeted NIRS) only.

During the observed VMs without infiltration of the vasoconstrictor (as considered for comparison with the MRI data) the difference in recovered parameters observed in both channels from neurological (forehead) and somatic (zygoma) tissue were statistically significant ($P = 0.012$), with saturation decreasing during the VM at the forehead and increasing in somatic tissue (Tables 1 and 2).

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Table 1. Summary of mean peak saturation changes observed from measured forehead sites during a 10-s maximal VM. Mean calculated from 18 Valsalva maneuvers.

Brain targeted NIRS	Left side Saturation (Channel A)	Right side Saturation (Channel B)
Range	*−6.7 to + 2.68%*	*−8.04% to + 2.3%*
Average	*−1.59%*	*−1.7%*
Median	*−1.7%*	*−1.73%*

Table 2. Summary of mean peak saturation changes observed from measured somatic site during a 10-s VM. Mean Calculated from 18 Valsalva maneuvers.

Somatic targeted NIRS	Left side Saturation (Channel A)	Right side Saturation (Channel B)
Range	*−1.31 to + 10.6%*	*+1.79 to + 8.27%*
Average	*+4.54%*	*+3.52*
Median	*+5.02%*	*+3.19%*

After the application of vasoconstrictor, largely similar results were yielded in terms of response morphology during the VM (Table 3). No statistically significant differences were observed between the maximum changes in saturation from the brain targeted NIRS pre- and post-infiltration ($P = 0.123$ Channel A, $P = 0.093$ Channel B) (Fig. 8). The effect of infiltration on the skin was quantified by laser Doppler and was found to be largely in keeping with previous reports in the literature, with a consistent decrease in flux observed between 40 and 85% (mean ± SD: 55 ± 15%) (Fig. 9).

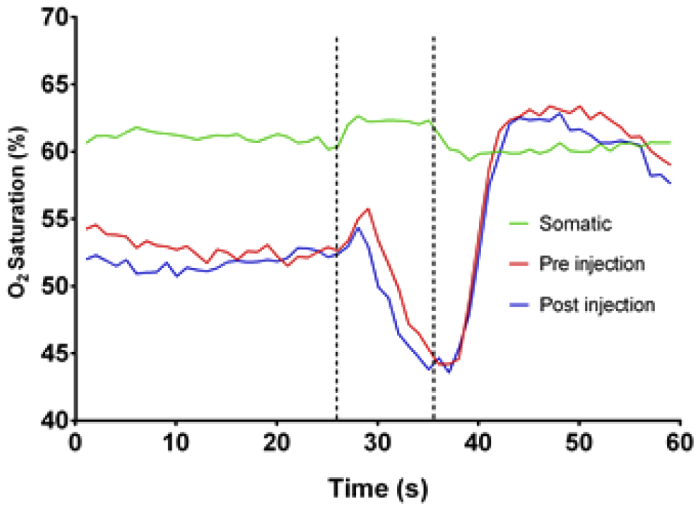

Fig. 8. A representative illustration of oxygen saturation derived by the ISS NIRS system from one participant during 10-s Valsalva maneuvers with NIRS targeted at brain (pre- and post-injection of vasoconstrictor) and somatic tissue. Dotted lines represent period of maximal Valsalva.

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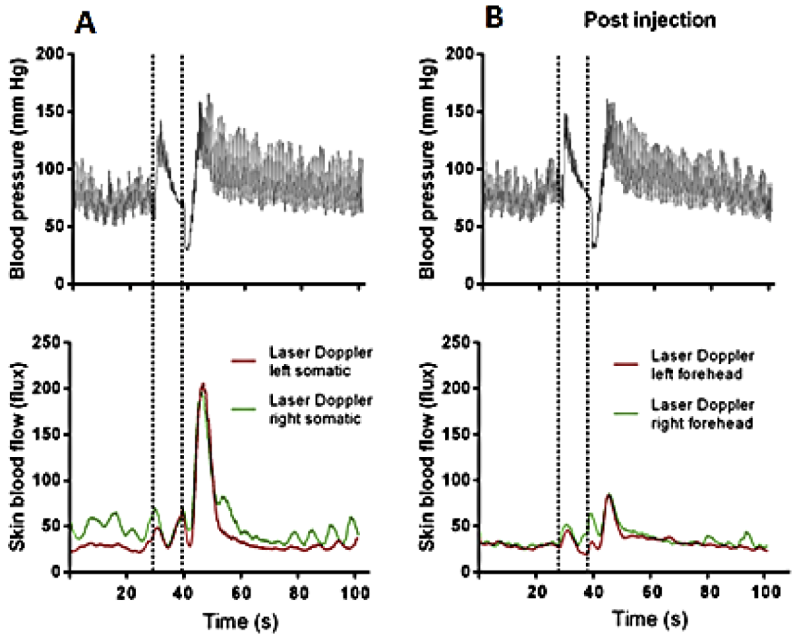

Fig. 9. A representative illustration from one participant of the effect of vasoconstrictor on Laser Doppler parameters during a 10-s Valsalva recorded on forehead tissue following injection (right side) compared to that recorded from somatic tissue (left side). Dotted lines represent period of maximal Valsalva. A) Blood pressure and skin laser Doppler response during VM without vasoconstrictor. B) The same responses after application of vasoconstrictor. Note the consistency in the 4-phase blood pressure response to maximal exertion Valsalva.

Table 3. Summary of mean peak saturation changes observed from measured forehead sites during a 10-s Valsalva maneuver following infiltration of vasoconstrictor. Mean values calculated from 17 Valsalva maneuvers.

Brain Directed NIRS	Left side Saturation	Right side Saturation
After infiltrating skin vasoconstrictor	(Channel A)	(Channel B)
Range	*−4.4% to + 1.85%*	*−8.11% to + 0.25%*
Average	*−1.08%*	*−2.06%*
Median	*−1.43%*	*−1.38%*

5. Discussion

This investigation set out to demonstrate that a carefully executed maximal effort Valsalva has the ability to induce haemodynamic changes in the brain and superficial tissues that clearly resolve one from the other. The difference in morphology of NIRS signal from zygomatic and frontal sources, together with the corresponding MR derived data confirms this clearly. Generally, during VM (specifically the period in which high thoracic pressure is being maintained) superficial tissue saturation increases or potentially remains consistent, whereas the brain experiences a reduction in saturation. Defining the dynamic separation of haemodynamic behaviour between the intra and extra cranial tissues during a maximal exertion VM is potentially the key novel output of this investigation.

From this separation of activity we can support the use of this technique as a potential validation tool for NIRS aiming specifically at cerebrally derived parameters. Wu et al demonstrated in

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their 2015 investigation a similar fMRI BOLD morphology to VM to what we have observed [18]. In their investigation an exhalation pressure of 30mmHg was sufficient to demonstrate a brain derived reduction in signal during pressurisation in line with our hypothesis. This may be a sufficient intrathoracic pressure to induce the changes we have described. However, extracranial data was not derived in their experiment and therefore the separation of activity that we have aimed to demonstrate was not observed.

This investigation has demonstrated that both the FD-NIRS device tested and fMRI have similar abilities in monitoring changes during VM both within and outside of the skull. The data highlighting that intracranially both modalities are likely to be deriving their data from similar sources with good correlation between parameters during Valsalva, and a robust cross correlation was demonstrated in all our comparisons.

The addition of a vasoconstrictor into the skin did not significantly change the underlying signature of the Valsalva from brain tissue. This may indicate that within this context with a significant (maximal exertion Valsalva) stimulus applied the change in proportion of contribution to the output parameters of the superficial tissue is not sufficient to effect the overall changes seen.

Franceschini et al used a version of this device to obtain reflective quantitative values for oxygenated and deoxygenated haemoglobin (utilising 8 emission wavelengths instead of the standard 2) from a group of healthy neonates [19]. This modification afforded a greater degree of redundancy as more measurements reduce the overall impact of any single erroneous reading. If such a system was employed a potentially clearer resolution between tissues may have been observable. However, a key facet of our investigation was to investigate the abilities of this device in its unmodified 'as purchased' state (2 wavelengths only), as it is in this configuration that the device is currently available to clinicians and clinical scientists alike. As a point of translation; an investigator or healthcare professional using this device may ask the observed individual to perform a VM (or initiate a VM themselves in the intubated patient). Should they observe a general desaturation during pressurisation then it may be reasonable to assume that the activity observed is predominantly brain derived.

An investigation in 2013 by Tsubaki et al utilised the Valsalva to highlight how significant changes in blood pressure effect NIRS output parameters in both the brain and overlying superficial tissues [14]. They demonstrated that the Valsalva provoked a change in the relative baseline parameters from each (a change in the difference between the two at baseline). An importantly different observation from our study is that a Valsalva causes an almost polar opposite NIRS parameter signature in each tissue. Our use of a maximal effort Valsalva as oppose to a specific forced expiratory opposition pressure [15,19] will have potentially contributed to the identification of this. As sufficient intrathoracic pressure to overcome venous outflow may be a key feature of what is required to reproduce our observed activity.

Other important investigations into the isolation of task based cerebral activity from that of superficial extracranial tissue by waveform analysis have previously described how the increased water content and architecture of the later contributes to the reduced BOLD signal observed [20]. In order to minimise this effect Tachtsidis et al ensured placement of the BOLD acquisition voxel within the vascular hypodermis of the skin overlying cortical tissue [20]. These observations were incorporated into our MR acquisition planning. However, we still observed a significantly lower signal change within our extracranial fMRI measurements (S.D of change 3.45% vs. 1.46% within the group for cerebral and extracranial respectively).

6. Conclusion

A maximal effort Valsalva maneuver in healthy individual has the ability to induce physiological changes that clearly differentiate brain from extracranial tissue. This is clearly confirmed by both fMRI and NIRS observations. It is likely to be due to the effect of the greater metabolic

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requirements of cerebral tissue within the context of venous congestion and falling perfusion pressure with an enclosed calvarium.

The FD-NIRS device used in standard form demonstrated equal ability to fMRI in differentiating between brain and extracranially derived activity and the significant reduction in superficial tissue perfusion by the addition of 1:100,000 adrenaline did not significantly change the signal observed.

Disclosures

The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

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