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Research Article

A Feasibility Study on the Efficacy of Functional Near-Infrared Spectrometry (fNIRS) to Measure Prefrontal Activation in Paediatric HIV

Sizwe Zondo,[1,2] **Aline Ferreira-Correia**,[2] **and Kate Cockcroft**[2]

[1]*Department of Psychology, Rhodes University, 1 University Road, Grahamstown 6139, South Africa*
[2]*Department of Psychology, University of the Witwatersrand, 1 Jan Smuts Avenue, Johannesburg 2000, South Africa*

Correspondence should be addressed to Sizwe Zondo; s.zondo@ru.ac.za

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Human immunodeficiency virus (HIV) infection is associated with disturbed neurotransmission and aberrant cortical networks. Although advances in the imaging of brain microarchitecture following neuroHIV has added to our knowledge of structural and functional changes associated with HIV, no data exists on paediatric HIV using optical neuroimaging techniques. This study investigated the feasibility of optical neuroimaging in paediatric HIV using functional near-infrared spectrometry (fNIRS). We measured prefrontal brain activation while participants executed a sustained attention task. We specifically tested whether patients living with HIV and study controls could perform the study protocol and whether we could measure the typical fNIRS haemodynamic response associated with neuronal activity. Eighteen participants (10 HIV participants, mean age: 13.9, SD = 1.66 years; 8 controls, mean age: 14.8, SD = 1.28 years), matched for sex, grade, and socio-economic status, were included in the study. All participants completed the Stroop colour word test (SCWT). Oxygenated haemoglobin concentration and the deoxygenated haemoglobin signal were recorded from the dorsolateral prefrontal cortex and the frontopolar area (FA) using fNIRS. The control group performed significantly better in terms of reaction time on the congruent and incongruent condition (congruent: t (16) = −3.36, $p < 0.05$: incongruent: $p < 0.05$). A pooled group analysis of the sample indicated significant activation in the DLPF and FA to the congruent condition of the SCWT ($p < 0.05$). Although cortical activation was noted in the DLPF and the FA in each of the groups when analysed independently, this neural activation did not reach statistical significance. The results show promise that fNIRS techniques are feasible for assessing prefrontal cortical activity in paediatric HIV. Future studies should seek to reduce the signal-to-noise ratio and consider inter-individual variability when measuring prefrontal activation in paediatric samples.

1. Introduction

The human immunodeficiency virus (HIV) continues to be a significant global pandemic, despite medical advances, such as haematopoietic stem cell transplantation [1, 2] and "shock and kill" gene transcription strategies [3, 4] to cure the disease. Figures of UNAIDS [5] indicate that by the end of 2022, approximately 38.4 million people were living with the virus, with 1.3 million newly reported cases of HIV in 2021 alone [5]. HIV is a ribonucleic acid (RNA), positive sense, enveloped, and single-stranded retrovirus [6]. The virus targets T cells that have differentiated into CD8 (cytokine) or CD4 (helper cell) cells. HIV primarily targets CD4+ T cells by binding to the protein gp120 that is found in its envelope. The gp120 protein further binds to either CXCR4 coreceptors or CCR5 coreceptors. HIV then injects its single strand of RNA into T cells and uses the enzyme reverse transcriptase to transcribe a complementary strand of proviral DNA.

Consequently, HIV infects the DNA of the host and replicates itself into the genetic material of its host. Over time, HIV further depletes CD4 cells, leading to HIV/AIDS [6, 7]. Through a mechanism yet to be understood, HIV is able to, almost immediately, permeate the blood–brain barrier and enter the brain through the differentiation of monocytes into macrophages [8]. Research suggests that macrophages infect other cells in the CNS, such as microglia and astrocytes [9, 10]. Thus, microglia and macrophages are thought to be cellular reservoirs for

HIV, allowing the virus to further replicate within the CNS, eventually affecting the integrity of nerve cells associated with neurocognition [7, 11, 12].

Although neurones do not express CD4 cells, HIV is believed to influence neural transmission in the nervous system [13, 14]. The impact of HIV on neural transmission is important, as neuronal networks are the basic foundations of cognitive processes within the cerebral cortex. Neuropathogenic studies, for example, reveal that HIV affects catecholaminergic neurotransmission. Catecholamines are derived from the amino acid tyrosine and include the neurotransmitters dopamine, norepinephrine, and epinephrine. Collectively, catecholamines are thought to be responsible for cognition, in particular, higher order abilities such as executive functions and sustained attention [15–17], and their dysregulation in the CNS, through HIV infection, is thought to affect these cognitive functions. Collectively, cognitive deficits consequent to HIV infection are referred to as HIV-associated neurocognitive disorder (HAND) [13].

Given the above neuronal dysregulation, quantifying the effect of the virus within the cerebral cortex is integral, both for nosology and therapeutic objectives. Hitherto, neuroimaging studies, including functional magnetic resonance imaging (fMRI) [18, 19], positron emission tomography (PET) [20], diffusion tensor imaging (DTI) [21], proton magnetic resonance spectroscopy (MRS) [22] and magneto-electroencephalography (MEG) [23], have provided valuable biomarker data into the structural and functional pursuance of HIV in the cerebral cortex. For example, fMRI neuroimaging has evidenced brain atrophy and cortical thinning in the frontal cortices of HIV+ participants, which is associated with dysexecutive functions in people living with HIV [18]. Similarly, PET studies using brain radioligands have indicated chronic activation of microglia cells, leading to neuroinflammation in cortical regions such as the frontal, parietal, and basal ganglia, which are thought to contribute to neurocognitive disorders observed in HAND [20, 24].

Similarly, MRS neuroimaging studies have indicated increased metabolite concentrations of membrane markers (Cho, Mi) whose elevation in HIV reflects inflammation and demyelination in microglia, which in turn are associated with the neurocognitive decline observed in neuroHIV [22]. Analogously, DTI indicates that compared to healthy controls, HIV-positive children (HAART-naïve and slow progressors) display lower fractional anisotropy, indicative of lower white matter integrity in the corpus callosum, internal capsule, and superior longitudinal fasciculus. Demyelination in these cortical regions is associated with poor performance in various neuropsychological assessments, including executive functions, attention, and processing speed [21].

Although neuroimaging techniques provide invaluable insight into cortical macroarchitecture sequent HIV neuroinvasion, these techniques tend to be inaccessible and less practical in low-resource settings due to the elevated and operational costs associated with their implementation [25, 26]. Secondarily, PET, fMRI, and MEG techniques have intrinsic limitations. For example, PET requires using radioisotopes, which have perceived radiation hazards [27]. MRI and MEG require participants to remain restrained while completing neuropsychological assessments, making them unsuitable for use with children [25]. Given these limitations, advances in neuroimaging technology allow the investigation of neurocognition using optical neuroimaging in the form of functional near-infrared spectrometry (fNIRS). The latter are portable neuroimaging devices that provide a high measure of spatial specificity in cortical function at a relatively low cost [28–30].

fNIRS brain imaging techniques use light to collect data related to superficial cortical haemodynamic activity [31]. Contextually, light is fragmented into multiple wavelength spectra (the wavelength spectrum includes gamma rays, X-ray ultraviolet, infrared, microwave, short radiowave, and long-radio wave) that represent colour. fNIRS neuroimaging uses light in the near-infrared (NIR) spectrum range (650–950 nm) (red light) to detect the concentration of oxygenated haemoglobin (HbO) and deoxygenated haemoglobin (deoxy-Hb), activated within the cortex in response to neuronal activation [31] (light in the near-infra range spectrum (650–950 nm) passes human tissue at relatively high intensity and is more likely to be detected by light detectors. An additional property of NIR light is that it is less absorbed by other body tissues in the body, other than hemoglobin [30, 32]). As a biosensor, fNIRS measures the interaction between light and matter and how much of the light is absorbed by haemoglobin—a metalloprotein that transports oxygen from the alveolus to the rest of the body via red blood cells [33]. Within the cerebral cortex, neuronal cells carry oxygenated haemoglobin or deoxygenated haemoglobin.

fNIRS neuroimaging, therefore, seeks to gather brain activity by measuring changes in haemodynamic responses, as indicated by changes in the concentration of haemoglobin protein in neuronal cells [30]. In their application, fNIRS elicit cortical activation by emitting NIR light through sources and detectors attached to fNIRS neuroimaging devices [30]. Correspondingly, increased cortical activity within neuronal cells increases metabolic demand for oxygenated blood (greater haemoglobin) juxtaposed with a decrease in deoxygenated blood. Summarily, optical neuroimaging techniques, in the form of fNIRS, use optical properties of light to capture the amount of haemoglobin present within neuronal cells, which indicates the brain's response to cognitive and cortical activity.

A recent systematic review [34] indicates a paucity of neuroimaging studies in paediatric HIV. This is due to multiple factors, not limited to but including the limited availability of appropriate imaging techniques for this population and the cost limitations previously noted. Given the above limitations, this pilot study sought to explore the feasibility of using fNIRS neuroimaging to investigate cortical activation in paediatric HIV. Our study specifically focused on assessing prefrontal activation during the execution of a sustained attention task, the Stroop colour word test (SCWT).

First, to answer the question of fNIRS feasibility, we explored participants' reported comfortability and ease of completing the study protocol whilst wearing the fNIRS neuroimaging device. Second, we measured various primary indexes related to fNIRS signal quality, including (a) scalp coupling index (SCI) [35], (b) wavelength synchrony [35],

(c) spike removal [36], (d) typical haemodynamic response (i.e., an increase in HbO, and a decrease in deoxy-Hb) [32], and (e) task-dependent vascular coupling due to completing the SCWT.

The SCI measures the quality of the light transmission and light detection of the optodes (sources and detectors) as they are coupled to the skin, namely the scalp. It is based on the cross-correlation across measurements of the fNIRS signal (760 and 690 nm) in relation to the frequency range of the cardiac signal [35]. Significantly, the SCI can be affected by multiple factors, including coarse hair, skin pigmentation, and optode pressure—the former factors are important to be aware of when working with African participants, as in our study [35]. Results from the SCI are interpreted in that the higher the correlation coefficient, the better the optode-scalp coupling within a particular channel of interest. Channels below a threshold of ($SCI < 0.75$) indicate a greater signal-to-noise ratio and are consequently excluded from further processing in the fNIRS general linear model [35].

We chose to limit our feasibility study to the prefrontal lobes since HIV predominantly affects the central executive network (CEN; anterior frontal lobes, dorsolateral prefrontal cortex (DLPFC), inferior parietal, and temporal regions) [18, 21, 37–39], leading to executive dysfunction and impairments in attention and working memory (among the areas of interest in our main study). Our pilot focused on key nodes within the CEN, namely the anterior frontal lobes and DLPFC, while participants completed the SCWT. The SCWT has previously been used to study attention and executive functions in paediatric HIV [40–43] and neural activation of the DLPFC (Brodmann's area [9, 44]) in healthy subjects (e.g., [45]). The SCWT has successfully been paired with fNIRS neuroimaging to investigate, for example, (a) the effect of attention workload [44], (b) the effects of meditation on sustained attention [46], (c) the effects of traumatic brain injury (TBI) on selective attention and response inhibition [47], and (d) the effects of caffeine on sustained attention [48]. Given the previous indications to evoke the haemodynamic response in the prefrontal and DLPFC, we selected the SCWT as the assessment choice for our feasibility study.

2. Materials and Methods

2.1. Participants. Purposive sampling was used to recruit 18 participants from a shelter caring for children living with HIV. Ten of the research participants were children living with HIV, whereas the remaining eight were HIV-negative. All participants were indigenous right-handed Africans (in this context, "indigenous African" refers to Black Africans of sub-Saharan Africa descent, with brown/dark skin pigmentation and dark, curlier hair [49]), aged between 12 and 16 years of age ($M = 14.28$, $SD = 1.53$) and were attending either primary or secondary schooling at the time of the study. Participants living with HIV were enrolled in the study if they were on a course of HAART therapy. Participants were excluded from the study if they presented with (a) auditory deficits, (b) visual impairments, (c) TBI, and (d) other CNS-related ailments (e.g., cerebral palsy, meningitis, or other neurological diseases). Written informed consent was obtained from the directors of the shelter and, where possible, from the children's guardians. Assent was obtained from all participants. Ethical approval for this study was granted by the University of the Witwatersrand's Human Ethics Committee (M211073). Equator reporting standards for conducting and reporting neuroimaging research can be found under (Supplementary File 1).

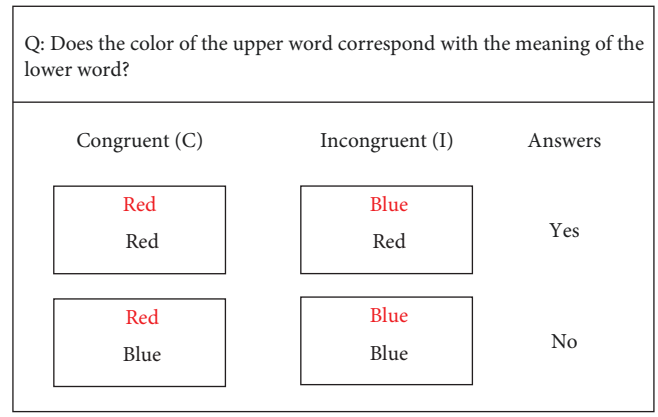


Figure 1: The Stroop colour word test. *Note*. The SCWT was adapted from Schroeter et al. [51].

2.1.1. Demographic Questionnaire. A *Demographic Questionnaire* completed by the director/guardian collected data concerning age, gender, education, HIV status, and other relevant information related to the inclusion and exclusion criteria.

2.1.2. Behavioural Assessment. Participants completed a computerised version of the SCWT, built using PsychoPy [50], to measure sustained attention. Our SCWT took the form of an fNIRS block design (we adopted the block design procedure as opposed to the event-related designs. The former has been indicated to show stronger statistical power and elucidate greater haemodynamic responses [32]) adapted from Schroeter et al. [51]. In the classical SCWT, a colour word, such as blue, is written in an ink colour, which may or may not be the same as the colour word. First, the participant must name the colour of the word, while ignoring the actual word. Then, the participant must read the word and ignore the colour [52, 53]. The Stroop interference effect occurs when reading the word interferes with naming the colour (incongruent condition). Generally, the interference effect requires greater attentional capacity. It has been correlated with slower responses, less accuracy, and greater cortical activation of the CEN attuned to higher cognitive functions, including executive functions and attention [51, 54].

In the SCWT used in our study, participants were required to answer the following question: "*Does the colour ink of the top word match the meaning of the bottom word*?". As indicated in Figure 1, two conditions were implemented to answer this question, namely, Condition 1, which was a congruent block (the colour of the top word was the same as the meaning of the bottom word), and Condition 2, which was an incongruent block (colour of the top word differed from the meaning of the bottom word).

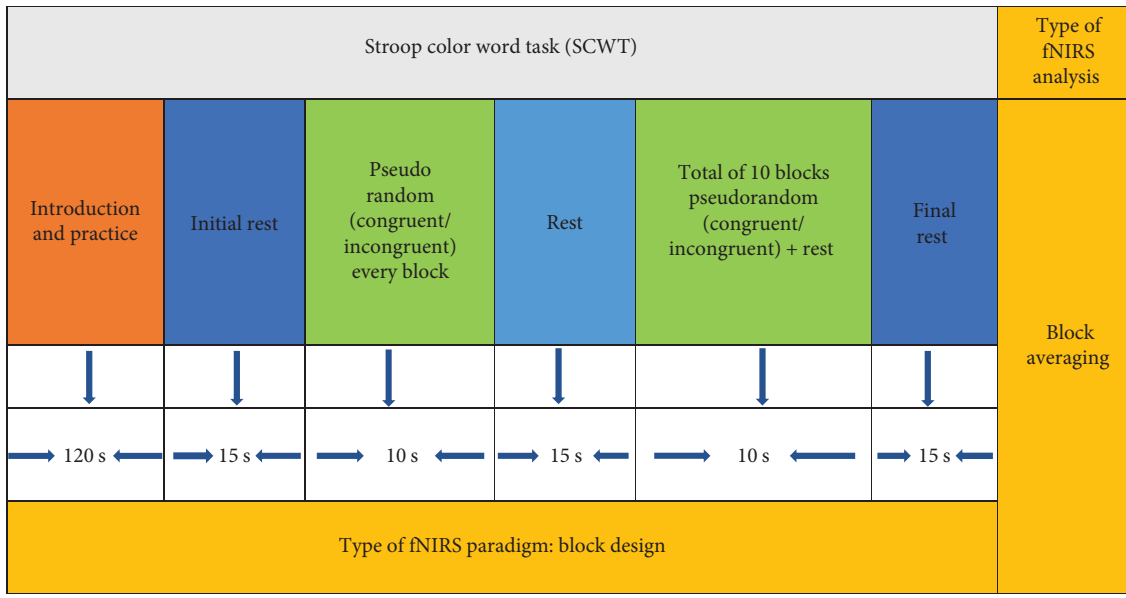


Figure 2: The Stroop colour word block design. *Note.* An fNIRS block average design was applied to analyse the SCWT. In total, 10 blocks (five congruent and five incongruent) lasting 10 s each were interspaced with 15 s of rest.

As indicated in Figure 2, each block (congruent, incongruent) was presented five times for a maximum of 10 blocks. Each block was interspaced with 15 s of rest, during which participants had to stare at a "+" sign before responding to the block condition. Event markers (triggers) built on PsychoPy required participants to press *q* on the computer keyboard in response to congruent stimuli and *p* in response to incongruent stimuli. Participants were first presented with a paper version of the SCWT for practice purposes before completing the test version for neuroimaging purposes (Supplementary File 1). In total, the SCWT took 8 min to complete.

2.2. fNIRS

2.2.1. Data Acquisition. The NIRxSport2 (NIRx, Medical Technologies, Berlin), a portable, wearable, multichannel fNIRS system, measured concentration changes in HbO and deoxy-Hb while participants completed the SCWT. As indicated in Figure 3, we used 8×7 optode arrays covering the prefrontal cortex for our study. Eight LED emitters consisting of two NIR light sources, with 760 and 850 nm wavelengths, were placed on positions AF3, AF7, Fz, F3, AF4, AF8, FpZ, and F4. LED emitters were paired with seven photodiode detectors to capture LED light placed on positions F1, Fp1, F5, F6, AFz, Fp2, and F2 of the fNIRS cap. The placement of sources and detectors corresponded with underlying cortical regions concentrated in Brodmann areas 9, 10, 45, and 46. The Broadman areas, covering the frontopolar prefrontal cortex and DLPFC, have been implicated in the cortical activation of executive functions and sustained attention [55–57].

Probe placement (sources and detectors) to identify the location of the above-predefined regions was determined using the "fNIRS Optodes Location Decider" (fOLD) software [58] (please see Supplementary File 1). In total, we investigated 22 channels covering the prefrontal cortex. The distance between sources and detectors was 2.5 cm, following guidelines for data acquisition with paediatric samples [59]. Signal calibration and recording of fNIRS data was done using Aurora 1.4. Acquisition Software (v2021.9, Medical Technologies, Berlin). Data were recorded at a sampling frequency rate of 7.85 Hz, based on two wavelengths, 760 and 850 nm.

2.2.2. Borg Rating of Perceived Exertion (RPE): Feasibility Assessment. To judge the feasibility of the protocol, participants were asked to complete two measures. In the first task, the participant completed the Borg rating of the PRE scale [60]. The Borg scale has been used in other fNIRS feasibility studies [61] to measure the PRE of any physical task on a scale from 1 (really easy) to 10 (really really hard). Participants also completed a 5-point Likert-scale questionnaire based on their experience with the fNIRS system. The questionnaire included two primary questions: "Did the fNIRS system (NIRXSport2) burden you while completing the cognitive activity?" (1 = "No, not at all" and 5 = "Yes, a lot") and "Could you complete the cognitive activity?" (1 = "Yes, very easily do-able" and 5 = "No, undoable"). All questions were asked in either isiXhosa or isiZulu, two indigenous languages spoken in South Africa or in English.

2.2.3. Procedure. All participants were tested independently in a secure research laboratory in the Department of Psychology at Rhodes University. The laboratory was equipped with a desk, computer, and chair. Upon arrival, participants were first seated at a desk equipped with a computer (screen diameter: 22 cm; height: 33.2 cm) and were requested to complete an assay of protocols. First, to confirm information gathered during the recruitment phase of the study, participants were asked to verify their demographic details. Thereafter, the participant information sheet was read to participants, which was proceeded by participants reading and signing the informed assent sheet. Once these assays

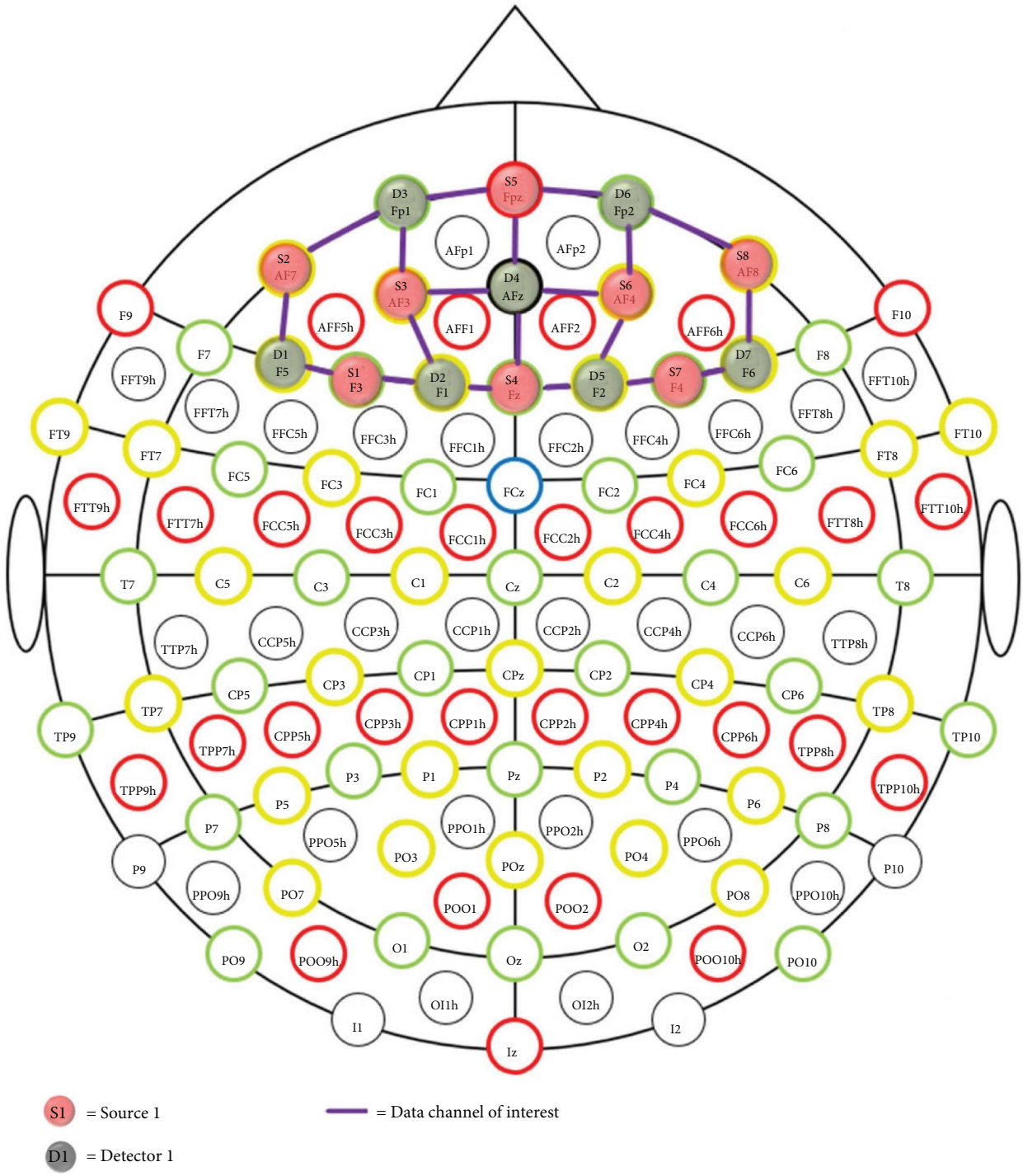


Figure 3: Regions of interest for optode placement. *Note*. Regions of interest for our study covered the frontopolar and dorsolateral prefrontal cortex (DLPFC).

were complete, participants completed the fNIRS protocol as detailed below.

2.3. fNIRS Cap Placement. A red marker was first used to note the "Fpz" optode position to assist with placing the fNIRS cap. The location of the "Fpz" was followed by cranial measurements, using a measuring tape, to establish the preauricular points and the distance from the nasion to the inion. Once these fiducial points were established, the researcher (SZ) fitted the fNIRS cap onto the research participants (see Figure 4). The fNIRS neoprene head cap with optodes was then covered with an overlayer cap to prevent external light from affecting the fNIRS signal. When all signals and channels were deemed acceptable, as indicated by Aurora Software, administration of the SCWT commenced. In total, the entire protocol took 25–30 min to complete.

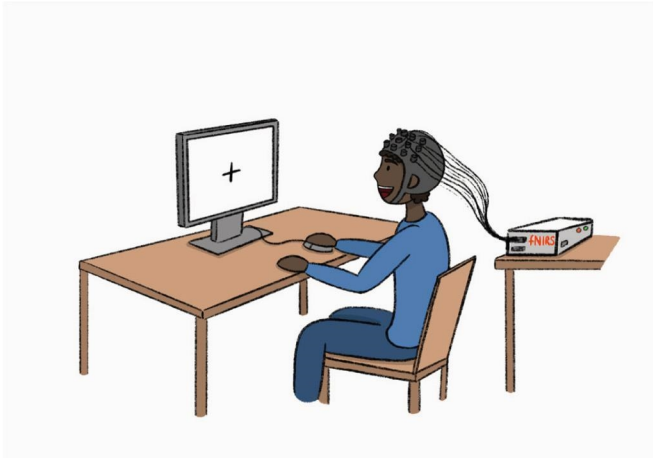


Figure 4: Seating position of research participant with fNIRS cap. *Note*. Participant seating position while completing the SCWT coupled with fNIRS neuroimaging. Copyright: Laura Bell & Sizwe Zondo.

2.3.1. Data Signal Preprocessing. The analysis of fNIRS data was executed on Satori fNIRS (NIRX Software, Brain Innovation, BV, Netherlands). Channel rejections were applied based on the SCI = 0.75 [62]. Motion artefacts, including head movement, were corrected by applying spike removal parameters based on monotonic interpolations [36]. Spike removal corrections were followed by temporal derivative distribution repair (TDDR) to remove baseline shifts and spike artefacts in the data [63]. Low-frequency band-pass filtering was applied to eliminate baseline drift on the data. Physiological fluctuations related to blood pressure fluctuations (1–1.5 Hz) and respiration (0.2–0.5 Hz) were removed using low-pass (LP) and high-pass Butterworth filtering. In this manner, the LP filter (0.1–0.2 Hz) enabled further removal of high-frequency noise within the data that was not accounted for by brain activity [64]. The high pass filter (0.01 Hz) was applied to attenuate low-frequency signals by removing baseline drift that may have affected the haemodynamic signal. Once data were preprocessed, changes in light intensity were converted into concentration changes in Oxy-Hb and deoxy-Hb, using the Modified Beer–Lambert Law.

3. Results

3.1. Demographic Data. Table 1 summarises the demographic characteristics of the sample. Chi-squared tests revealed no significant differences in sex ratio, $\chi^2 = 0.22$, $p = 0.63$, and schooling level, $\chi^2 = 2.00$, $p = 0.16$. There were, however, significant differences in the sample based on the age index, $\chi^2 = 13.6$, $p = 0.004$.

Table 1: Demographics characteristics ($N = 18$).

Sample characteristics	HIV group		Control group		Full sample	
	n	%	*n*	%	*n*	%
Sex						
Male	5	27.8	3	16.7	8	44
Female	5	27.8	5	27.8	10	56
Age range (years)						
10 −12	2	11.1	0	0	2	11
12–14	2	11.1	2	11.1	4	22
14–16	6	33.3	5	27.8	11	61
16–18	0	0	1	5.6	1	6
Ethnicity						
IsiXhosa	9	50	8	44	17	94
Other languages	1	5.6	0	0	1	6
School						
Primary	2	11.1	4	22.2	4	22
Secondary	8	44	4	22.2	14	78

3.2. Feasibility Measures

3.2.1. Borg Ratings. Most participants (83.3%) reported that they could complete the study protocol. On average, participants' scores ($M = 3.83$, SD = 1.34) on the Borg CR10, corresponded to a fairly light physical exertion for all study protocols. Concerning completing the SCWT whilst fitted with the NIRXSport2, participants reported that the device did not burden them whilst undertaking the SCWT ($M = 2.28$, SD = 1.02). Participants further indicated that the cognitive task (SCWT) was *easily doable* ($M = 2.61$, SD = 1.29).

3.2.2. fNIRS Measures.
(1) SCI Measures. Results of the SCI analysis (Figure 5) indicated that when we set a threshold of SCI < 0.75, 80% of channels in our study were rejected, and 20% were retained. The average SCI for the combined sample (HIV participants and controls) of our study was SCI = 0.45.

3.2.3. Wavelength Data. Figure 6 represents raw wavelength data. Raw wavelength explorations analyse the time course of the two fNIRS wavelengths, 760 and 850 nm. Within the fNIRS data, synchronous behaviour should be noted between the wavelengths, which corresponds with the SCI measure [35]. For feasibility purposes, we indicate the sufficiency of this criterion by representing synchrony in channels S5–D4 and S8–D5 of Participant 1. Importantly, we noted synchrony in all raw wavelength analyses (760 and 850 nm) for each of our participants in our feasibility study ($n = 18$).

3.2.4. Spike Removal. We further analysed feasibility by measuring motion artefact corrections by applying the spike removal method, which is applied before TDDR algorithm corrections to process signal data. As indicated in Figure 7, we were able to identify and remove several "spikes" within our data channels (e.g., S6–D6) using *z*-score spike detection methods, as suggested by van Brakel [36]. This finding illustrates that for our sample of interest, we were able to correct motion artefacts without exacerbating baseline shifts within our data, thus allowing for a more robust statistical analysis to be carried out using general linear modelling.

3.2.5. Event-Related Averages. Lastly, we undertook feasibility measures by analysing event-related averages due to cortical activation while completing the SCWT. Several channels in

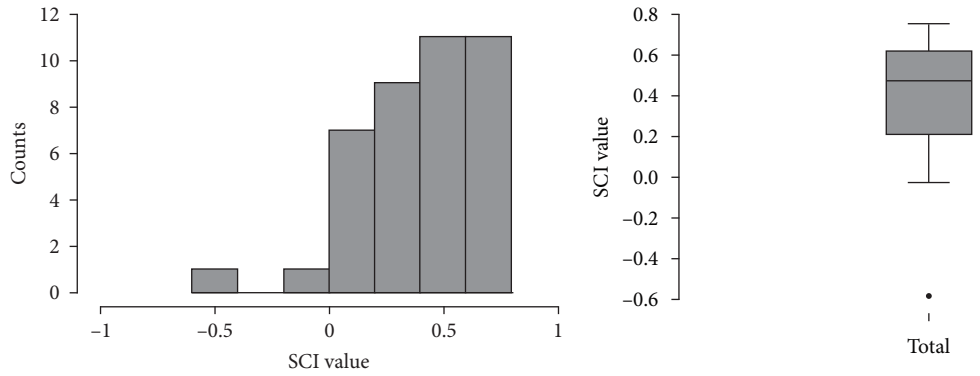


Figure 5: Scalp coupling index: (a) scalp coupling index (0.75) (indicates the distribution of scores); (b) scalp coupling index (0.75) (indicates the Boxplot of all SCI scores, with one outlier in the data). SCI for all participants in the study was = 0.45.

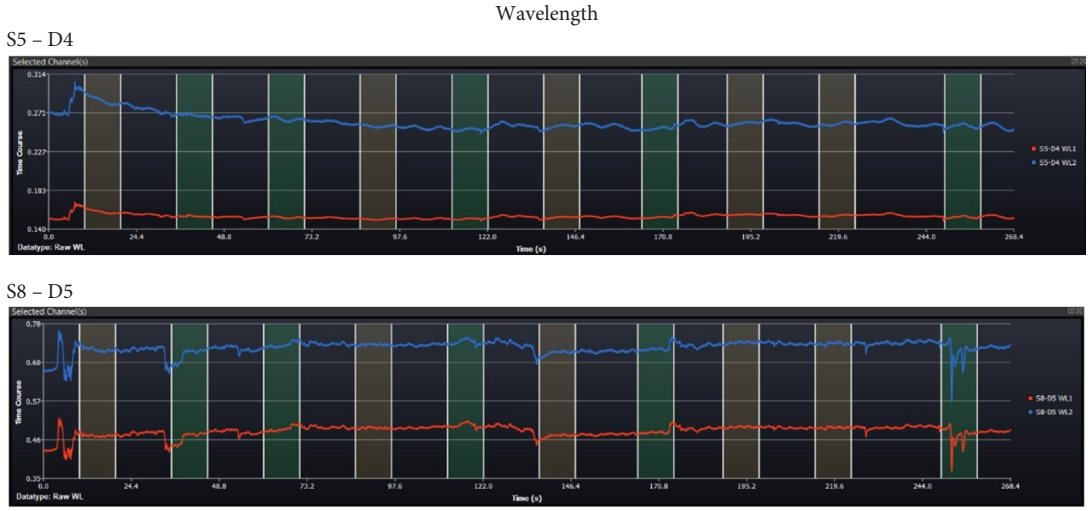


Figure 6: Wavelength synchrony for participant 1 at two wavelengths, 760 and 850.

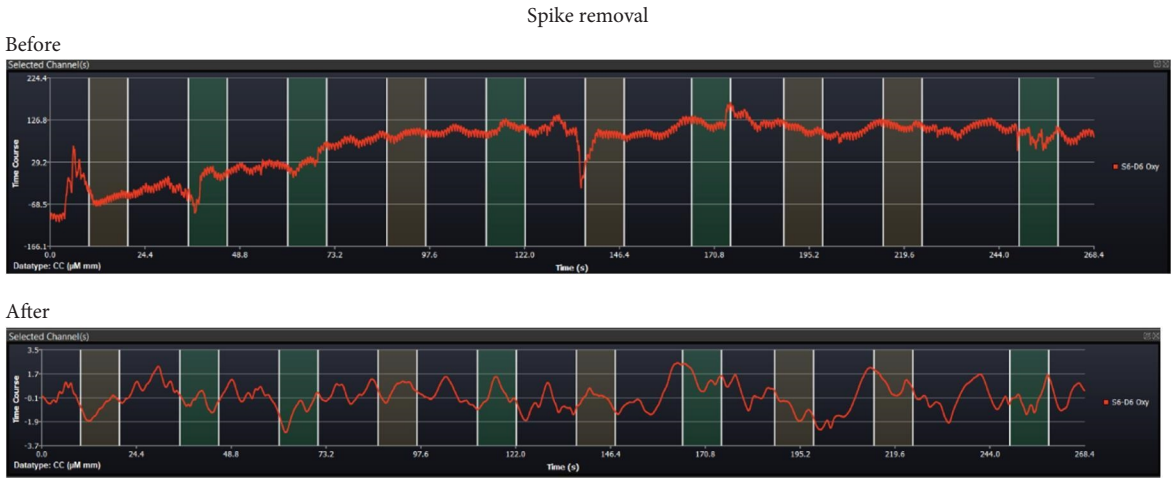


Figure 7: Effect of fNIRS spike removal indicating motion artefact corrections.

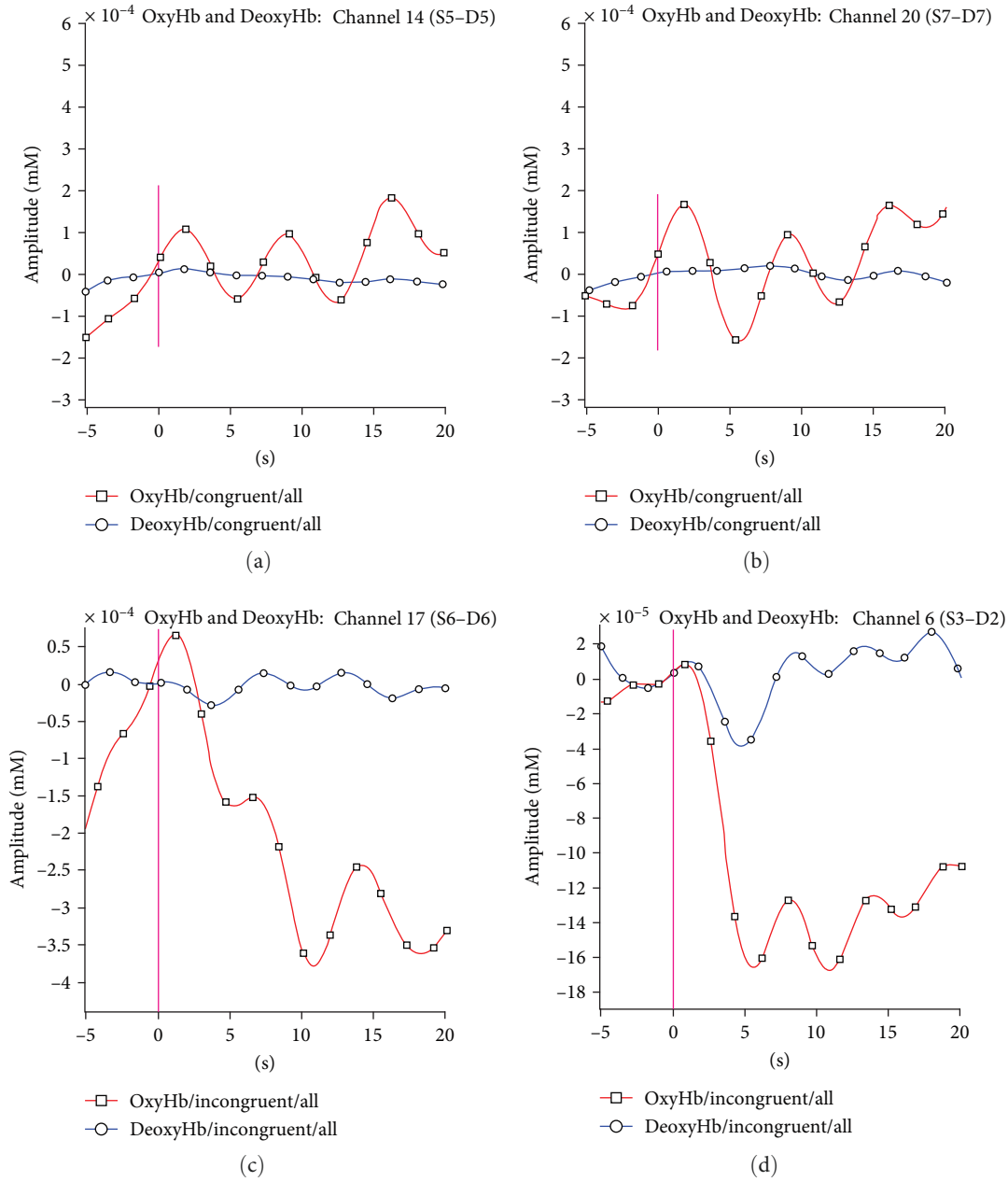
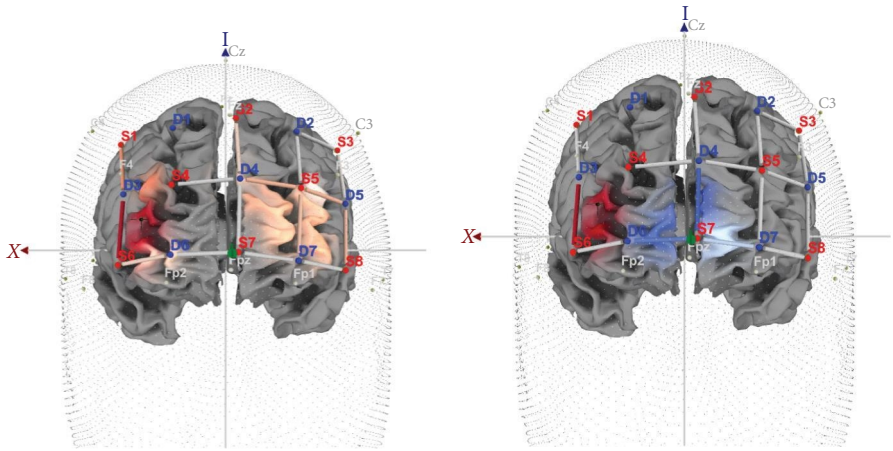


Figure 8: Event-related averages for congruent vs. baseline and incongruent vs. baseline: (a) event-related average (congruent); (b) event related average (congruent); (c) event-related average (incongruent); (d) event-related average (incongruent). (a) and (b) Indicate the typical haemodynamic response in the congruent condition (increase in HbO relative to a decrease in deoxy-HbO). The typical haemodynamic response was not always evident in the incongruent vs. baseline condition (c and d).

the feasibility study indicated expected task-dependent relative increases of oxygenated haemoglobin relative to a decrease or stable level of deoxygenated haemoglobin [31]. For example, Figures 8(a) and 8(b) (Participant 1) indicate the expected relative increases in HbO relative to a decrease in HbO during the congruent vs. baseline task (channels, S5–D5, S7–D7). Nonetheless, our feasibility study indicated atypical haemodynamic responses in the incongruent vs. baseline condition (e.g., Figures 8(c) and 8(d)) in several participants.

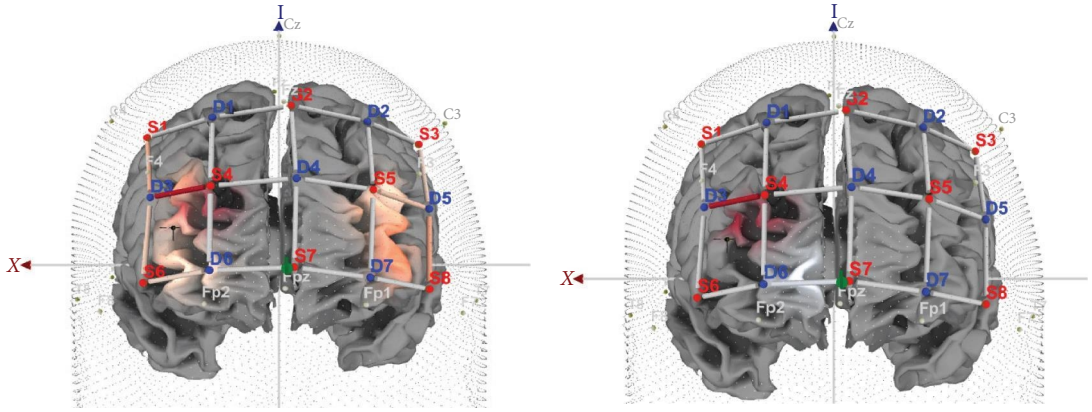
3.2.6. fNIRS Results.

(1) PFC Brain Activation (Group Analysis). Brain activation is indicated using T-statistics maps for HbO. T-maps were conducted at three levels: (1) for the entire sample, (2) for the HIV group, and (3) for the control group. We compared brain activation for congruent vs. baseline and incongruent vs. baseline activation. The combined sample demonstrated significantly greater HbO increases in the congruent vs. baseline condition. Brain activation was noted in the bilateral



(a) (b)

Figure 9: Task vs. baseline measures T maps (entire sample): (a) congruent vs. baseline (statistically significant differences ($p<0.05$) were noted for the congruent vs. baseline condition in the prefrontal cortex); (b) incongruent vs. baseline (although there was activation in the incongruent vs. baseline comparison, this was not significant ($p>0.05$).



(a) (b)

Figure 10: Task vs. baseline measures T maps (HIV group): (a) congruent vs. baseline (HIV group) (the prefrontal region showed strong activation in the congruent vs. baseline condition for the HIV group, this activation did not reach statistical significance ($p>0.05$)); (b) incongruent vs. baseline (HIV group) (there was markedly diminished cortical activation in the incongruent vs. baseline ($p>0.05$) for the HIV group).

DLPFC and VLPFC, with greater activation in the right hemisphere (Figure 9(a)). The latency peak of HbO activity in this condition indicated brain activation on several channels (4, 7, 8, and 12), resulting in significant t-map activations ($p<0.05$) in this condition. Although brain activation was noted in the right hemisphere for the incongruent vs. baseline condition, the latency to the peak of HbO activity did not reach significance ($p>0.05$; Figure 9(b)).

(2) PFC Brain Activation: HIV Group. During the congruent condition, the HIV group demonstrated bilateral brain activation in the DLPFC and VLPFC for the congruent vs. baseline condition. The latency to the peak of HbO activity during this condition did not reach statistical significance ($p>0.05$; Figure 10(a)). As indicated in Figure 10(b), there was markedly diminished cortical activation for the incongruent vs. baseline condition in most channels within the HIV group.

(3) PFC Brain Activation: Control Group. During the congruent condition, the control group demonstrated bilateral brain activation in the VLPFC for the congruent vs. baseline condition. The latency to the peak of HbO activity during this condition did not reach statistical significance ($p>0.05$; Figure 11(a)). Diminished cortical activation was noted for the incongruent vs. baseline condition in most channels, resulting in insignificant t-map activations ($p>0.05$; Figure 11(b)).

(4) PFC Brain Activation: HIV Group Compared to Control Group. In addition to the above, we compared the two groups on the latency to the peak of HbO on the congruent vs. baseline and incongruent vs. baseline condition. No significant latency to peak differences were noted between the HIV and control groups on any of the conditions ($p>0.05$).

3.2.7. Behavioural Results. The results of the SCWT task are indicated in Table 2. During the congruent condition, the

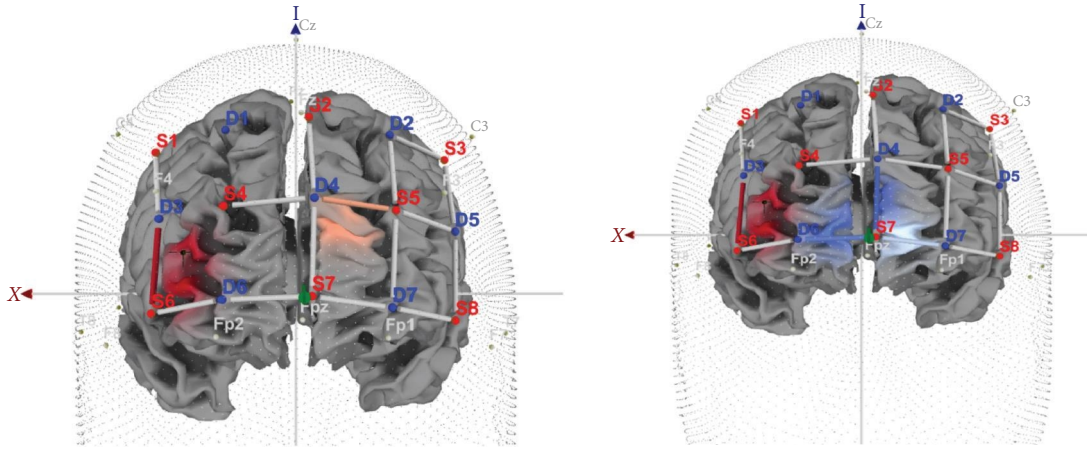


Figure 11: Task vs. baseline measures T maps (control group): (a) congruent vs. baseline (the prefrontal region showed strong activation in the congruent vs. baseline condition for the control group. This activation did not reach statistical significance ($p > 0.05$)); (b) incongruent vs. baseline (there was markedly diminished cortical activation in the incongruent vs. baseline ($p > 0.05$) for the control group).

Table 2: Stroop colour word test behavioural performance.

Condition	Response time (ms)				Accuracy (%)			
	Congruent		Incongruent		Congruent		Incongruent	
	M	SD	M	SD	M	SD	M	SD
HIV	3,585.48	932.38	4,336.10	1,038.76	0.826	0.062	0.601	0.189
Control	2,321.48	565.49	3,029.83	625.011	0.936	0.049	0.870	0.075

Note: Significant differences were noted in congruent and incongruent responses between the two groups.

HIV group was significantly slower at responding ($M = 3{,}585.48$; SD = 932.38) compared to the control group ($M = 2{,}321.48$; SD = 565.49) ($t(16) = -3.36$. $p < 0.05$). Similarly, the HIV group made significantly more errors ($M = 0.826$, SD = 0.062) compared to the control group ($M = 0.936$, SD = 0.049) ($t(16) = -4.11$, $p < 0.05$) for this condition. During the incongruent condition, the HIV group was also significantly slower ($M = 4{,}336.10$, SD = 1,038.76) compared to the control group ($M = 3{,}029.83$, SD = 625.011) ($t(14) = -3.77$, $p < 0.05$). Additionally, the HIV group also made significantly more errors on this condition ($M = 0.601$; SD = 0.189) compared to the control group ($M = 0.870$; $SD = 0.07$) ($t(16) = -3.12$, $p < 0.05$).

4. Discussion

Research indicates frontostriatal and CEN aberrations due to HIV, subsequently leading to HAND [18, 21, 65]. There is a paucity of neuroimaging research investigating the effects of HIV on the cerebral cortex [34]. Cognisant of the dearth of neuroimaging studies in paediatric HIV, our study investigated the feasibility of fNIRS neuroimaging to measure prefrontal cortical activation in children and adolescents living with HIV. Findings suggest that optical imaging captured cortical activation in this population. Primarily, participants reported experiencing a low burden of the fNIRS devices whilst performing the SCWT cognitive task.

Significantly, visual inspection of the fNIRS signal indicated feasibility as indicated by acceptable, though low SCI measures, coupled with synchronous wavelength behaviour. Pointedly, fNIRS data indicated typical cortical activity patterns of increased oxygenated (HbO) and stable deoxygenated haemoglobin (deoxy-Hb) concentrations in several channels during the congruent vs. baseline condition. Although our study did not detect significant group differences between the HIV and control group, fNIRS neuroimaging was able to detect task-dependent changes in HbO (congruent vs. baseline, incongruent vs. baseline) within the HIV and control group as a cohort. These findings support the feasibility of using fNIRS neuroimaging techniques to measure sustained attention in the PFC, which is compromised in HIV [66, 67].

Although we could not detect significant neuronal differences between controls and HIV participants, at a cortical level, behavioural findings indicated significant differences between the groups on the SCWT. This is in line with previous studies [40, 68, 69]. Interestingly, although there were significant differences in the Stroop interference task between the groups, fNIRS neuroimaging indicated diminished cortical activation in both groups when completing the Stroop interference task relative to the congruent vs. baseline task. The interference tasks require a greater neuronal workload, leading to greater activation of the CEN [70, 71]. Given expected neuronal activation due to the interference task,

diminished cortical activation during the SCWT interference task may be indicative of SES-dependent prefrontal hypoactivation [72], with data suggesting that living in low SES environments may be linked with reduced cognitive stimulation [72–74], thus leading to diminished prefrontal activation.

Notwithstanding the above, although our feasibility study sought to control for the influence of hair density on the fNIRS signal by employing spring grommets, we did not control for superficial (e.g., skin) haemodynamics using short separation channels [59, 75]. There is evidence that epidermal pigments can potentially affect photon transmission in fNIRS in dark-skinned subjects, similar to our participants, leading to difficulty in detecting neuronal depolarisation when completing cognitive tasks [76, 77].

Sequel to the above, it is recommended that future fNIRS studies improve on our preliminary findings by applying various measures to study the haemodynamic response in the context of paediatric HIV. For example, although the placement of the fNIRS cap procedure was identical for all participants, as it was based on relative distances from external landmarks, namely, the nasion and inion, there is a small chance that cap placement might have targeted slightly different cortical regions due to morphological differences between participants. Future protocols could improve signal detection and subsequent SCI between tasks by adjusting the fNIRS device and using crochet hooks to gently adjust coarse hair until task-related cortical activity is observed and before commencing cortical measurement.

In addition to the above, research indicates interindividual differences in the neuropsychological and neurobiological sequelae of HIV [78, 79] based on divergent factors such as adverse childhood experiences, HIV genotype and phenotype, and commencement of HAART. It is recommended that future fNIRS studies investigating the effects of neuroHIV on cognition could benefit from larger samples. Although our sample size ($n = 18$) was sufficient to meet the primary objectives of conducting a feasibility study, the small sample was a limitation and prevented the implementation of robust statistical procedures to analyse the multiple variables that may affect the fNIRS haemodynamic response. Nonetheless, based on the mean difference in HbO concentrations between congruent and incongruent conditions in the present study, it was deemed that at least 42 participants would be needed to find significant differences in HbO concentrations between the cognitive tasks (power = 0.80, $\alpha = 0.05$, one-tailed testing).

5. Conclusions

To the researchers' knowledge, this is the first study to investigate the efficacy of fNIRS neuroimaging for a paediatric HIV sample, inclusive of participants of African descent. Findings suggest the feasibility of fNIRS to study frontal activation in both clinical and healthy children with dark pigmentation and curly hair who are under-represented in fNIRS research [77]. Most significantly, our findings imply that fNIRS may be used as a marker for frontal lobe in/efficiency in a cognitive rehabilitation setting at a relatively inexpensive cost.

Data Availability

All data used to support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Supplementary Materials

Supplementary File 1 includes the Stroop test, fOLD montage for fNIRS optode selection, and the Equator Reporting Standards for reporting neuroimaging data, which are available in the supplementary files document. (*Supplementary Materials*)

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