fNIRS: New ways to identify atypical patterns of prefrontal cortex activation in Autism Spectrum Disorder

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Introduction

- Prospective memory (PM) involves the interplay of several cognitive abilities, such as executive functioning and social cognition.
- Autism spectrum disorder (ASD) is characterized by abnormalities in these cognitive functions and, in particular, in time-based PM[1].
- The identification of a phenotype of ASD is extremely challenging since the spectrum is characterized by heterogeneity at the genetic, neural, and behavioural levels.

Aim

To investigate the feasibility of fNIRS in the classification of ASD based on hemodynamic, physiological and cognitive correlates of a time-based PM task using both conventional and novel approaches based on the General Linear Model (GLM).

Hypotheses:

1) Differences in the localization of brain activity to the PM task (higher lateral PFC activity to the PM task compared to the ongoing (OG) task[2])
2) Activation patterns reflecting increased heterogeneity within the ASD group
3) Differences in the fullfilment of delayed intentions between some ASD individuals and the typically developed control group

Materials and Methods

fNIRS and Physiological Data Acquisition

- A 16-channel fiberless and wearable fNIRS system (WOT, Hitachi High-technologies Corporation, Japan; sampling frequency=5 Hz) monitored prefrontal cortex activity (Figure 1).

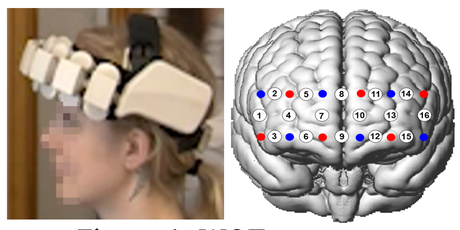

Figure 1. WOT system

Participants and Experimental Protocol

- 26 high-functioning ASD (age 33.0±10.4 years) and 27 typically developed (TD; 33.8±11.9 years) matched on verbal and performance IQ, were recruited.
- Participants were engaged in a time-based PM task (Figure 2). While performing the OG task (Figure 2 B), they had to press the spacebar on a computer keyboard every time they felt 30 s were passed (PM hit).

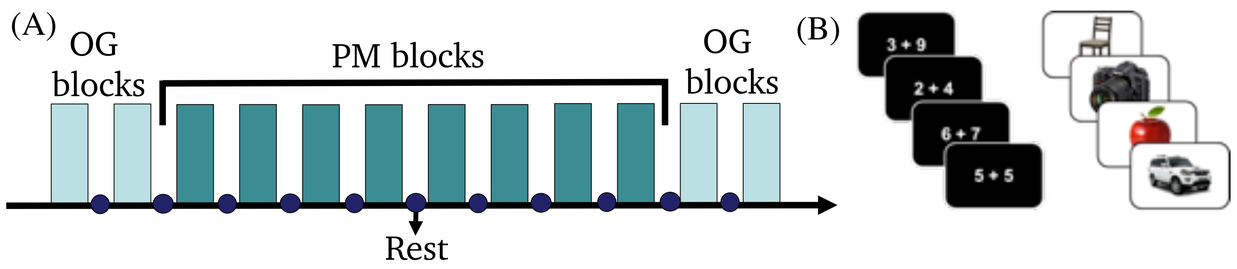

Figure 2. Experimental protocol (A) and Ongoing task (B).

fNIRS signal pre-processing analysis

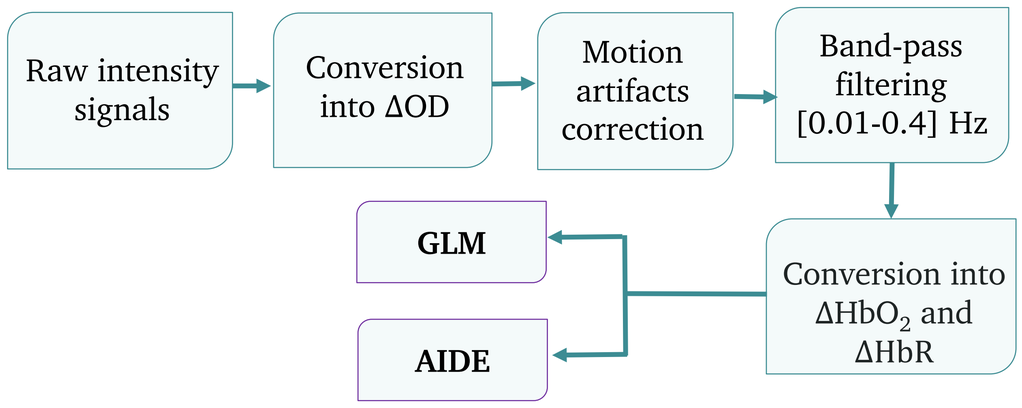

Figure 3. Oxy- (HbO_2) and deoxy- (HbR) hemoglobin signals pre-processing steps.

A conventional GLM approach was used to:

1) Statistically localise functional brain activity using the contrast PM>OG for the two groups individually

2) To run modified *t*-tests[2] on the estimated β-values to discriminate ASD participants at individual level respect to a normative healthy group to account for the heterogeneity within the ASD

AIDE[4] was used to:

3) investigate the differences between the two groups in the temporal distribution of functional activity due to PM events.

Results

Conventional GLM

1) Opposite activation patterns were found for the ASD group[2] (Table 1), with higher activation to the OG task in left PFC.

		TD (N=27)	ASD (N=26)	
		Ch. 2 (right PFC)		Ch. 16 (left PFC)
HbO_2	*t*-value	2,25	N.S.	-2,95
	p-value	0.04		0.008
			Ch. 13 (left PFC)	Ch. 16 (left PFC)
HbR	*t*-value	N.S.	-2,31	-1,98
	p-value		0.03	0.06

Table 1. Group significant channels ($p<0.05$) for the conventional GLM analysis.

2) We observed differences in activation patterns within the ASD group (Figure 4) reflecting the heterogeneity of individuals with ASD.

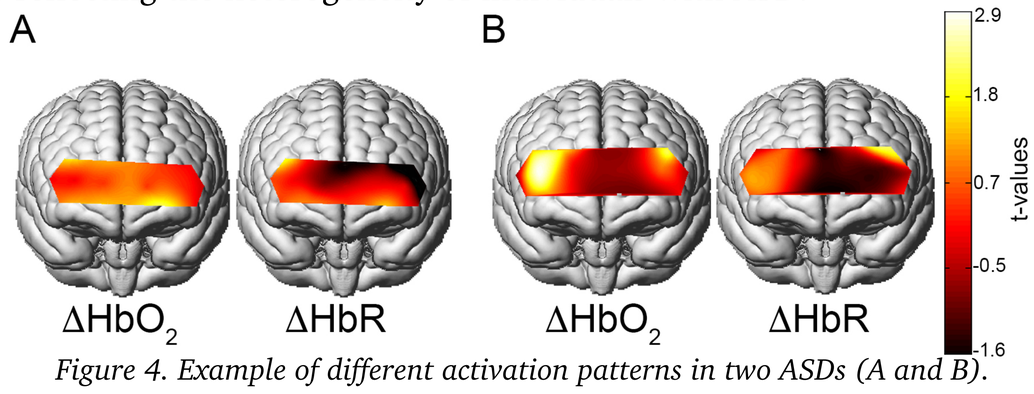

Figure 4. Example of different activation patterns in two ASDs (A and B).

The modified *t*-test revealed differences in 10 ASD participants respect to the normative TD group at single-subject level.

AIDE

3) AIDE recovered the onsets of functional events related to maintaining and fulfil the delayed intention from fNIRS data (Figure 5 A).

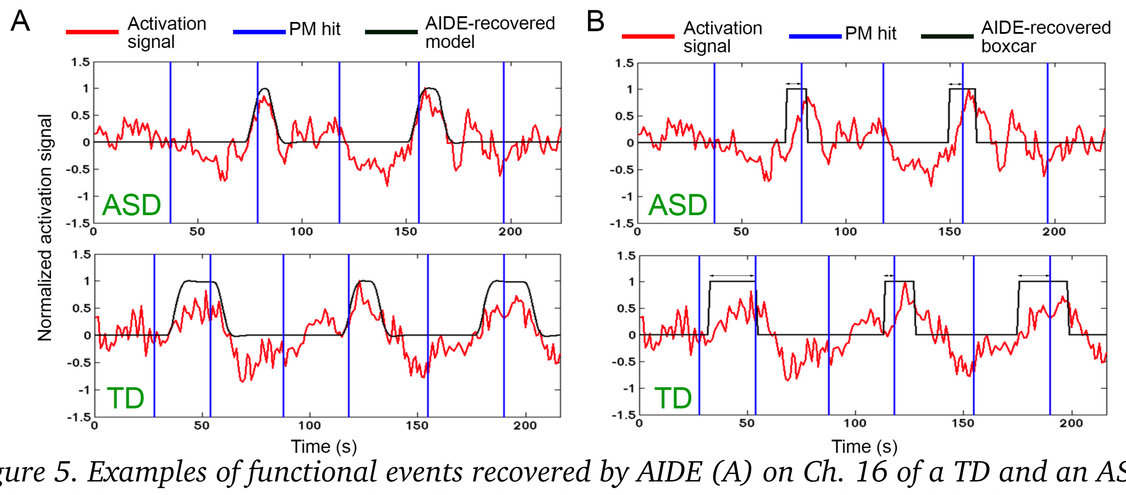

Figure 5. Examples of functional events recovered by AIDE (A) on Ch. 16 of a TD and an ASD. Time differences between the identified functional event onset and the PM hits (B, arrows) were evaluated.

Statistically significant differences in the time differences between the AIDE-identified functional event onset and the PM hits (Figure 5 B) were observed between the ASD and TD group.

Time delay ASD (s; mean±std)	Time delay TD (s; mean±std)	*t*-value
-2.73±3.28	-4.38 ±3.78	$t(50)=2.61$ ($p=0.01$)

Table 2. T-test results computed on the time differences between the identified functional event onset and the PM hits between the ASD vs the TD group.

Conclusions

1) fNIRS is suitable to unveil differences in the activation patterns of ASDs with respect to TDs (Figure 4), with opposite hemodynamic distribution in ASDs[2].
2) ASD is characterized by heterogeneity at cortical level and fNIRS could help in discriminating ASDs from TDs at single-subject level.
3) The brain-first approach provided by AIDE[4] is able to disentangle the functional activations related to the PM task, and to unveil the differences between TD and ASD (Table 2). The time difference between the PM hits and the AIDE-identified events for the TDs is similar to typical ~5s value and is smaller for the ASD.

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3. Crawford, J. R., & Howell, D. C. (1998). *The Clinical Neuropsychologist*, *12*(4), 482-486.
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